

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 June 2005 (06.01.2005)

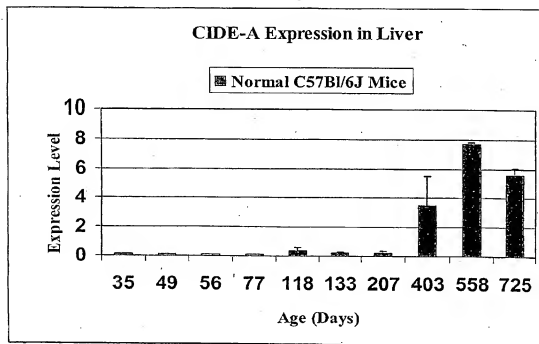
PCT

(10) International Publication Number  
WO 2005/000335 A2

- (51) International Patent Classification<sup>7</sup>: A61K 38/00. (74) Agents: BROWDY AND NEIMARK, P.L.L.C. et al.; 624 Ninth Street N.W., Suite 300, Washington, DC 20001-5303 (US).
- (21) International Application Number: PCT/US2004/017322
- (22) International Filing Date: 2 June 2004 (02.06.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/474,606 2 June 2003 (02.06.2003) US
- (71) Applicant (for all designated States except US): OHIO UNIVERSITY [US/US]; Technology Transfer Office, 20 East Circle Drive, Athens, 11 45701 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): KOPCHICK, John, J. [US/US]; 4 Orchard Lane, Athens, 36 45701 (US). KELDER, Bruce [US/US]; 346 Carroll Road, Athens, Ohio 45701 (US). BOYCE, Keith S. [US/US]; 2589 Cole Road, Wexford, Pennsylvania 15090 (US). KRIETE, Andres [US/US]; 1222 Driftwood Drive, Pittsburgh, Pennsylvania 15243 (US).
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: DIAGNOSIS AND TREATMENT METHODS RELATED TO AGING, ESPECIALLY OF LIVER



(57) Abstract: Mouse genes differentially expressed in comparisons of older and younger livers by gene chip analysis have been identified, as have corresponding human genes and proteins. The human molecules, or antagonists thereof, may be used for protection against faster-than-normal biological aging, or to achieve slower-than-normal biological aging. The human molecules may also be used as markers of biological aging.

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

DIAGNOSIS AND TREATMENT METHODS RELATED TO AGING, ESPECIALLY  
OF LIVER

This application claims the benefit, under 35 USC 119(e), of  
U.S. Provisional application 60/474,606, filed June 2, 2003,  
which is hereby incorporated by reference in its entirety.

*Cross-Reference to Related Applications*

*Anti-Aging Applications.* Mice with a disrupted growth  
hormone receptor/binding protein gene enjoy an increased  
lifespan. In U.S. Prov. Appl. 60/485,222, filed July 8,  
2003 (Kopchick8) mouse genes differentially expressed in  
comparisons of gene expression in growth hormone  
receptor/binding protein gene-disrupted mouse livers and  
normal mouse livers were identified, as were corresponding  
human genes and proteins. It was suggested that the human  
molecules, or antagonists thereof, could be used for  
protection against faster-than-normal biological aging, or  
to achieve slower-than-normal biological aging. It was also  
taught that the human molecules may also be used as markers  
of biological aging.

In provisional application Ser. No. 60/566,068, filed  
April 29, 2004 (our docket Kopchick14-USA), our research  
group used a gene chip to study the genetic changes in the  
muscle of C57Bl/6 mice that occur at various intervals of  
the aging process. Differential hybridization techniques  
were used to identify mouse genes that are differentially  
expressed in mice, depending upon their age. The level of  
gene expression of approximately 10,000 mouse genes ( from  
the Amersham Codelink UniSet Mouse I Bioarray, product  
code: 300013) in the muscle of mice with average ages of .35,  
49, 77, 118, 133, 207, 403, 558 and 725 days was determined.  
In essence, complementary RNA derived from mice of different  
ages was screened for hybridization with oligonucleotide  
probes each specific to a particular mouse gene, each gene

in turn representative of a particular mouse gene cluster (Unigene). Mouse genes which were differentially expressed (younger vs. older), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene, were identified. Related human genes and proteins were identified by sequence comparisons to the mouse gene or protein.

*Anti-Diabetes Applications.* In U.S. Provisional Appl. Ser. No. 60/458,398 (our docket Kelder1-USA), filed March 31, 2003, members of our research group describe the identification of genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse liver. Forward- and reverse-subtracted cDNA libraries were prepared; clones were isolated, and differentially expressed cDNA inserts were sequenced and compared with sequences in publicly available sequence databases. The corresponding mouse and human genes and proteins were identified.

The purpose of our research group's provisional application Ser. No. 60/460,415 (our docket: Kopchick6-USA), filed April 7, 2003, was similar, but complementary RNA, derived from RNA of mouse liver, was screened against a mouse gene chip. See also 60/506,716, filed Sept. 30, 2003 (Kopchick6.1).

Gene chip analyses have also been used to identify genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse pancreas, see U.S. Provisional Appl. 60/517,376, filed Nov. 6, 2003 (Kopchick12) and muscle, see U.S. Provisional Appl. 60/547,512, filed Feb. 26, 2004 (Kopchick15).

*Other differential hybridization applications.* The use of differential hybridization to identify genes and proteins



is also described in our research group's Ser. No. PCT/US00/12145 (Kopchick 3A-PCT), Ser. No. PCT/US00/12366 (Kopchick4A-PCT), and Ser. No. 60/400,052 (Kopchick5).

All of the foregoing applications are hereby incorporated by reference in their entirety.

## BACKGROUND OF THE INVENTION

### Field of the Invention

The invention relates to various nucleic acid molecules and proteins, and their use in (1) diagnosing aging, or adverse conditions associated with the aging process, and (2) protecting mammals (including humans) against the aging process or adverse conditions associated with the aging process.

### Description of the Background Art

The mechanisms that cause aging (the decline in survival and reproductive ability with advancing age) have puzzled our society and scientific community for centuries. The two major theories center on the question of whether normal aging is an evolutionarily-genetically preprogrammed pathway of internal changes or is a normal consequence of existence where there is an accumulation of molecular and cellular damages. Hypotheses of such accumulated damage include free radical-oxidative damage, defective mitochondria, somatic mutations, progressive shortening of telomeres, programmed cell death, impaired cell proliferation and numerous others (1). The current belief is that aging is not a programmed process in that, to date, no genes are known to have evolved specifically to cause damage and aging. The one factor that has been shown to extend the lifespan in organisms from yeast to mice has been a reduction in caloric intake (2, 3). Recent data suggests that caloric restriction may also be relevant for primates, including humans (4-6). Unfortunately, it is unlikely that

most people will be able to maintain the strict dietary control required to reap the benefits of this finding. Therefore, since the mechanism(s) by which caloric restriction extends lifespan are unknown, the elucidation of such mechanisms could lead to the development of alternative strategies to yield similar benefits.

Numerous groups are presently engaged in identifying genes and pathways that are involved in the aging process. A growing list of genes that extend adult longevity have been identified and a large proportion of these genes are involved with hormonal signals. Many of these genes and the corresponding endocrine systems are conserved among a wide variety of eukaryotes. What is becoming clear, at least in lower animal species, is that those pathways that provide advantages to development and growth early in life may impart negative consequences in later life. The clearest example of a genetic pathway affecting adult lifespan has been described in the nematode, *Caenorhabditis elegans*. When food is abundant, *C. elegans* develops directly to the reproductive adult through four larval stages in three days. Under adverse conditions such as caloric restriction or high population density, *C. elegans* enters the Dauer diapause, a non-feeding, stress-resistant larval state. Genetic analysis has identified that mutation of single genes involved in dauer formation (Daf) greatly extend the adult lifespan (7). These genes involve the highly-conserved insulin/IGF-like signal transduction pathway. Ligand binding to the *daf-2* insulin-like receptor results in a kinase signaling cascade to phosphorylate the forkhead transcription factor, *daf-16*. This phosphorylation sequesters *daf-16* to the cytoplasm and results in reproductive maturity and aging. In the absence of ligand and signal transduction, the unphosphorylated, *daf-16* localizes to the nucleus and regulates the transcription of its target genes that promote dauer formation, stress resistance and extended longevity (8). A similar pathway

has been described in *Drosophila melanogaster*. Mutation of the gene encoding insulin-like receptor (*InR*) or the gene encoding insulin-receptor substrate (*chico*) also extends the normal life-span (9,10). Vertebrate homologues of *daf-16* down-regulate genes promoting cell progression, induce genes involved in DNA-damage repair and up-regulate genes that reduce intracellular reactive oxygen species (ROS) (11,12). A second *C. elegans* gene, *clk-1*, has also been linked to the reduction of ROS and an extended life-span. While the effect of *daf-2* mutants result in a reduction of mitochondrial ROS, *clk-1* mutants reduce extramitochondrially produced ROS. Since the majority of cellular ROS is produced in the mitochondria during the process of electron transport, it is not surprising that *clk-1* mutants have only a moderately extended life-span. *C. elegans* containing *daf-2/clk-1* double mutations, however, exhibit a very long life-span (13).

Decreased IGF-1 signaling may also extend longevity in mice. Four mouse models with deficiencies in pituitary endocrine action have demonstrated retarded aging. In the *Prop1* and *Pit1* models, pituitary production of growth hormone (GH), prolactin (PRL) and thyroid stimulating hormone (TSH) are ablated. These mice have reduced growth rates, reduced adult body size and live 40 to 60% longer than normal mice (14,15). Unfortunately, it is not possible to determine which of the ablated hormones is responsible for the increased longevity of the models.

A more straightforward model was developed that targeted the deletion of the growth hormone receptor (*GHR-KO*) (16). This mouse line was derived from a founder animal by homologous recombination resulting in deletion and gene substitution of most of the fourth exon and part of the fourth intron of the *GHR/BP* gene. These mice also exhibit reduced body size and extended life-span and more directly implicates the GH/IGF-1 axis (17, 17a). Recently, evidence for a direct role of IGF-1 receptor signaling in affecting

the aging process was provided by the targeted disruption of the IGF-1 receptor (*Igf1r*) (18). Heterozygous females, but not males, possess 50% fewer receptors for IGF-1, live 33% longer than wild-type females and also display greater resistance to oxidative stress. Tyrosine phosphorylation of the intracellular signaling molecule, *Shc*, was also decreased in the *Igf1r*<sup>+/-</sup> females. Mice containing the targeted deletion of *p66shc* also have increased resistance to oxidative stress and a 30% increase in life span (19). While the IGF-1 axis appears to be involved in the aging process, the mechanism by which it does so remains unknown. However, these findings demonstrate that it is possible to identify specific genetic pathways that affect the aging process. The finding that caloric restriction of these mouse models can further extend their life-span suggests that multiple pathways exist that affect the aging process (20). Therefore, research to identify these pathways and the genes involved in the aging process is of great importance.

The role of growth hormone in aging is further discussed in Vance, ML, "Can Growth Hormone Prevent Aging," New Engl. J. Med., 348: 779-80 (Feb. 27, 2003).

#### **Gene-Chip Based Identification of genes involved in aging of liver**

Several groups have begun to utilize DNA microarrays to measure differences in gene expression caused by the aging process. However, these experiments are extremely limited in regards to the number of aging time points or experimental conditions.

Cao, S.X., et al., "Genomic profiling of short- and long-term caloric restriction effects in the liver of aging mice", Proc. Natl. Acad. Sci. USA, 98:10630-10635 (2001) used Affymetrix microarray technology to study the changes in expression levels of 11,000 genes in liver tissue of 7

month-old mice compared to 27 month-old mice. In this analysis, the expression of 20 genes increased at least 1.7-fold with age while the expression of 26 genes decreased at least 1.7-fold with age. We have compared the differentially expressed genes described by Cao et al., to those that we have found to be differentially expressed using the Amersham platform. Of the 20 up-regulated genes, 10 had links from Affymetrix to Amersham through Unigene. Only one of Cao's up-regulated genes, Heat shock protein (L07577/NM\_010410) was identified as differentially expressed in our analysis (increased 2.2-fold from weeks 2 to 4). Of Cao's 26 down-regulated genes, 10 had links from Affymetrix to Amersham through Unigene. Only one of these down-regulated genes (Mouse TIS21 gene, M64292/NM\_007570) was identified as differentially expressed in our analysis. However, we found the expression of this gene to increase 2.07-fold with age.

Tollet-Egnell, P., et al., "Gene expression profile of the aging process in rat liver: normalizing effects of growth hormone replacement, *Mol. Endocrinol.*, 15(2):308-18 (2001) used microarray technology to study the effect of aging and growth hormone treatment on the expression of 3,000 different genes in the rat liver. The proteins which were over-expressed in the older rat were glucose-6-phosphate isomerase (x1.8), pyruvate kinase (x4.8), hepatic product spot 14 (2.4x), fatty acid synthase (1.9x), staryl CoA desaturase (1.7x), enoyl CoA hydratase (1.7x), peroxisome proliferator activated receptor- $\alpha$  (1.7x), 3-ketoacyl-CoA thiolase (1.7x), 3-keto-acyl-CoA peroxisomal thiolase (1.9x), CYP4A3 (3.3x), glycerol-3-phosphate dehydrogenase (1.7x), NADPH-cytochrome P450 oxidoreductase (4.7x), CYP2C7 (1.9x), CYP3A2 (2.8x),  $\Delta$ -aminoevulinate synthase (2.3x). The under-expressed proteins were glucose-6-phosphatase (0.3x), farnesyl pyrophosphate synthase (0.5x), carnitine octanoyltransferase (0.5x), mitochondrial genome (16S ribosomal RNA) (0.3x), mitochondrial cytochrome c

oxidase II (0.4x), mitochondrial NADH dehydrogenase SU 5 (0.3x), mitochondrial cytochrome b (0.4x), mitochondrial NADH dehydrogenase SU 3 (0.5x), NADH-ubiquinone oxidoreductase (SU CI-SGDH and SU 39kDa) (both 0.5x), ubiquinol-cytochrome c reductase (Rieske iron-sulfur protein and core 1) (both 0.5x), CYP2C12 (0.4x), cystathione  $\gamma$ -lyase (0.3x), biphenyl hydrolase-related protein (0.5x), glutathione S-transferase (class pi) (0.3x),  $\alpha$ -1 macroglobulin (0.5x), BRAK related protein (0.3x),  $\alpha$ -2u-globulin (0.4x), cAMP-dependent transcription factor MAFK (0.5x), DAP-like kinase (0.5x), PCTAIRE-1 (0.5x), collagen  $\alpha$ -1 (0.4x), histone H2A (0.5x), and S-100 protein  $\alpha$  (0.5x).

Of the genes up-regulated in the older rat according to Tollet-Egnall, two have mouse cognates which we found to be up-regulated in the mouse liver. These were fatty acid synthase and stearyl CoA desaturase. A third, aminoevalinate synthase, has a mouse cognate which we found to be down-regulated in the older mouse. Two genes found by Tollet-Egnall to be down-regulated in the older rat were found by us to have cognates down-regulated in the older mouse: carnitine octanoyltransferase and CYP2C12.

See also Dozmorov I, Bartke A, Miller RA, "Array-based expression analysis of mouse liver genes: effect of age and of the longevity mutant Prop1<sup>df</sup>", J. Gerontol., 56A: B52-57 (2001). Liver mRNA levels were measured in Ames dwarf mice (homozygous for the df allele at the Prop1 locus; live 40% to 70% longer than nonmutant siblings) and in control mice at ages 5, 13 and 22 months. "The analysis showed seven genes where the effects of age reach  $p < .01$  in normal mice and six others with possible age effects in dwarf mice, but none of these met Bonferroni-adjusted significance thresholds. Thirteen genes showed possible effects of the df/df genotype at  $p < .01$ . One of these, insulin-like growth factor 1 (IGF-1), was statistically significant even after adjustment for multiple comparisons; and genes for two IGF-binding proteins, a cyclin, a heat shock protein, p38

mitogen-activated protein kinase, and an inducible cytochrome P450 were among those implicated by the survey. In young control mice, half of the expressed genes showed SDs that were more than 58% of the mean, and a simulation study showed that genes with this degree of interanimal variation would often produce false-positive findings when conclusions were based on ratio calculations alone (i.e., without formal significance testing). Many genes in our data set showed apparent young-to-old or normal-to-dwarf ratios above 2, but the large majority of these proved to be genes where high interanimal variation could create high ratios by chance alone, and only a few of the genes with large ratios achieved  $p < .05$ . The proportion of genes showing relatively large changes between 5 and 13 months, or from 13 to 22 months of age, was not diminished by the df/df genotype, providing no support for the idea that the dwarf mutation leads to global delay or deceleration of the pace of age-dependent changes in gene expression."

#### *Gene-Chip Based Identification of Genes Involved in aging of other organs and tissues*

Gene expression profiling has been performed on skeletal muscle tissue of mice at 5 versus 30 months of age with or without caloric restriction (21). In this analysis, the expression of 113 genes was found to be changes by at least two-fold in 5-month old mice compared to 30-month old mice. Caloric restriction of comparable mice caused a reversal of the altered gene expression of 33 genes. Similar analyses have also been performed on mouse brain and heart (22,23).

Weindruch, et al., "Microarray profiling of gene expression in aging and its alteration by caloric restriction in mice" in Symposium: Calorie Restriction: effects on Body Composition, Insulin Signaling and Aging

918S-923S (2001) (21) compared expression in gastrocnemius muscle from 5- and 30-month old C57BL/6 mice, with and without caloric restriction. In this analysis, the expression of 113 genes was found to be changed by at least two-fold in 5-month old mice compared to 30-month old mice. Caloric restriction of comparable mice caused a reversal of the altered gene expression of 33 genes.

Of the 6347 genes surveyed in the oligonucleotide microarray, only 58 (0.9%) displayed a greater than 2 fold increase in gene expression as a function of aging, whereas 55 (0.9%) displayed a greater than 2 fold decrease. Of the genes positively correlated with aging, 16% could be assigned to stress responses. The largest differential expression between young and aged animals (3.8 fold) was the mitochondrial sarcomeric creatine kinase.

Of the genes negatively correlated with aging, 13% were involved in energy metabolism. A noteworthy number were genes encoding biosynthetic enzymes (cytochrome P450 IIC12, squalene synthase, stearyl-CoA desaturase, EF-1-gamma. Another down regulator was a CpG binding protein, MeCP2.

Weindruch further reported that age-related changes in gene expression profile were "remarkably attenuated" by caloric restriction.

What appears to be the same experiment is discussed in Lee, et al., "Gene expression profile of aging and its retardation by caloric restriction," Science, 285: 1390 (Aug. 27, 1999). This paper lists the individual genes which were differentially expressed by more than 2-fold, and classifies them as energy metabolism, neuronal factors, protein metabolism, stress response, biosynthesis, calcium metabolism or DNA repair genes.

Welle, et al., "Skeletal muscle gene expression profiles in 20-29 year old and 65-71 year old women," Exper. Gerontol., 39: 369-77 (2004) and available electronically as doi:10.1016/j.exger.2003.11.011 studied gene expression and physical condition in seven young and eight older women.



With respect to physical condition, the measured or calculated parameters were total body mass, lean body mass, left leg lean mass (by biopsy), maximum isometric left knee extension force, left knee extension force/left leg lean mass, Peak  $\text{VO}_2$ /lean body mass, and Peak  $\text{VO}_2$ /left leg lean mass.

There were 1178 "probe sets" (representing 1053 different Unigene clusters) for which differential expression was detected; 550 for which expression was higher in older women, and 628 the inverse effect. The differences ranged from 1.2 to 4 fold; most (78A%) were less than 1.5 fold. The complete list of differentially expressed genes is given in the Rochester Muscle database website, [www.urmc.rochester.edu/smd/crc/swindex](http://www.urmc.rochester.edu/smd/crc/swindex) (".html" omitted, in accordance with USPTO requirements, so that the publication of this application will not create an active hyperlink).

The gene most highly overexpressed in older muscle was p21 (cyclin-dependent kinase inhibitor 1A) (4.01 fold). This one of several genes (see Welle Table 2) which are potentially related to DNA damage and repair. Welle also thought it noteworthy how many of the differentially expressed genes were ones that encode proteins which bind to pre-mRNAs or mRNAs (see Welle Table 3).

See also Lee et al., Science, 285 :1390-93 (1999) and Nature Genetics 25: 294-7 (2000) (bioarray study of changes in mouse cerebellum and neocortex to detect age-associated genes).

#### *Non-Gene Chip Differential/Subtractive hybridization studies*

The papers collected in this section deal principally with type II diabetes, which is an aging-related disease.

Sreekumar, et al., "Gene expression profile in skeletal muscle of type 2 diabetes and the effect of insulin treatment," *Diabetes* 51: 1913 (June 2002) surveyed 6,451 genes, and identified 85 genes for which there was an

12

alteration in skeletal muscle transcription in diabetic patients after withdrawal of insulin treatment. Subsequent insulin treatment resulted in further changes in transcription of 74 of the 85 genes (15 increased, 59 decreased), and also resulted in alteration of 29 additional gene transcripts.

Mootha, et al., "PCG-1 $\alpha$  responsive genes involved in oxidative phosphorylation are coordinatively downregulated in human diabetes," *Nature Genetics* 34(3); 267 (July 2003), used DNA microarrays to detect changes in the expression of sets of related genes, rather than of individual genes. They classified over 22,000 genes into 149 data sets; some of these data sets overlapped. They looked for a statistical correlation between the overall rank order of the genes in differential expression, and the groups to which the genes belonged. Expression was compared pairwise among three groups: males with normal glucose tolerance; males with impaired glucose tolerance; and males with type 2 diabetes. The set with the highest enrichment score (the one whose members ranked highly most often relative to chance expectation) was an internally curated set of 106 genes involved in oxidative phosphorylation. While the average decrease for the individual genes was modest (~20%), it was also consistent, being observed in 89% (94/106) of the genes in question. This paper is reviewed by Toye and Gauguier, "Genetics and functional genomics of type 2 diabetes mellitus", *Genome Biology*, 4: 241 (2003).

Patti, et al., "Coordinated reduction of genes of oxidative metabolism in humans with insulin resistance and diabetes: Potential role of PGC1 and NRF1", Proc. Nat. Acad. Sci. (USA), 100(14): 8466 (July 8, 2003) used microarrays to analyze skeletal muscle expression of genes in nondiabetic insulin-resistant subjects at high risk for diabetes (based on family history of diabetes and Mexican-American ethnicity) and diabetic Mexican-American subjects. Of 7,129 sequences represented on the microarray, 187 were differentially expressed between control and diabetic subjects. However, no single gene remained significantly differentially expressed after controlling for multiple comparison false discovery by using the Benjamini-Hochberg method, see Benjamini, et al., J. R. Stat. Soc. Ser. B. 57:289-300 (1995); Dudait, et al., Stat. Sin. 12: 111-139 (2002). Consequently, Patti et al. sought to identify groups of related genes with similar patterns of differential expression using MAPP FINDER and ONTOEXPRESS. According to MAPP FINDER, the top-ranked cellular component terms were mitochondrion, mitochondrial membrane, mitochondrial inner membrane, and ribosome, and the top-ranked process term was ATP biosynthesis. According to ONTOEXPRESS, the over-represented groups were energy generation, protein biosynthesis/ribosomal proteins, RNA binding, ribosomal structural protein, and ATP synthase complex.

Huang, Xudong, "Identification of abnormally expressed genes in skeletal muscle contributing to insulin resistance and type 2 diabetes", Thesis, document id: 9576 Lunds University 2002, reported differential expression of the mitochondrially-encoded ND1 gene in human diabetic patients and of the nuclear-encoded cathepsin L gene in mice.

Standaert, et al., "Skeletal muscle insulin resistance in obesity-associated type 2 diabetes in monkeys is linked to a defect in insulin activation of protein kinase C-

zeta/lambda/iota Diabetes 51: 2936 (Oct. 2002). the authors concluded that defective activation of atypical PKCs played an important role in the pathogenesis of peripheral insulin resistance in both obese prediabetic and diabetic monkeys.

They attributed this linkage to the apparent requirement for aPKCs during insulin-stimulated glucose transport.

Srommer, et al., Am. J. Physiol., "Skeletal muscle insulin resistance after trauma: insulin signaling and glucose transport", 275(2 Pt. 1): E3518 (Aug. 1998) concluded that insulin resistance in skeletal muscle after surgical trauma is associated with reduced glucose transport but not with impaired glucose signaling to PI 3-kinase or its downstream target, Akt.

Zhang, et al., Kidney International, 56:549-558 (1999) identified genes up-regulated in 5/6 nephrectomized (subtotal renal ablation) mouse kidney by a PCR-based subtraction method. Ten known and nine novel genes were identified. The ultimate goal was to identify genes involved in glomerular hyperfiltration and hypertrophy.

Melia, et al., Endocrinol., 139:688-95 (1998) applied subtractive hybridization methods for the identification of androgen-regulated genes in mouse kidney. The treatment mice were dosed with dihydrotestosterone, an androgen. Kidney androgen-regulated protein gene was used as a positive control, as it is known to be up-regulated by DHT.

See also Holland, et al., Abstract 607, "Identification of Genes Possibly Involved in Nephropathy of Bovine Growth Hormone Transgenic Mice" (Endocrine Society Meeting, June 22, 2000) and Coschigano, et al., Abstract 333, "Identification of Genes Potentially Involved in Kidney Protection During Diabetes" (Endocrine Society Meeting, June 22, 2000).

The following differential hybridization articles may also be of interest: Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys

15

undergoing glomerulosclerosis", *Kidney Int.*, 59:1363-73 (2001); Song, et al., "Cloning of a novel gene in the human kidney homologous to rat munc13S: its potential role in diabetic nephropathy", *Kidney Int.*, 53:1689-95 (1998); Page, et al., "Isolation of diabetes-associated kidney genes using differential display", *Biochem. Biophys. Res. Comm.*, 232:49-53 (1997); Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," *Kidney Int.* 53:926-31 (1998); Condorelli, *EMBO J.*, 17:3858-66 (1998);

See also Nadler, S.T., Stoehr, J.P., Schueler, K.L., Tanimoto, G., Yandell, B.S., Attie, A.D. (2000) "The expression of adipogenic genes is decreased in obesity and diabetes mellitus", *Proc Natl Acad Sci U S A* 97:11371-11376; Lan H, Rabaglia ME, Stoehr JP, Nadler ST, Schueler KL, Zou F, Yandell BS, Attie AD. (2003) "Gene expression profiles of nondiabetic and diabetic obese mice suggest a role of hepatic lipogenic capacity in diabetes susceptibility", *Diabetes* 52:688-700.

See also WO00/66784 (differential hybridization screening for brown adipose tissue); PCT/US00/12366, filed May 5, 2000 (differential hybridization screening for liver).

#### *Other Anti-Aging Studies*

For genes thought to have aging inhibitory activity, see generally International Longevity Center, Workshop Reports, "Longevity Genes: From Primitive Organisms to Humans," and "Is there an 'Anti-Aging' Medicine?".

Patents of possible interest include the following:

16

Lin, USP 6,303,768 (2001) ("Methuselah gene")

Lippman, USP 4,695,590 ("Method for retarding aging")

West, USP 6,368,789 (2002) ("Screening methods to identify inhibitors of telomerase activity")

### *Measurement of Biological Aging*

Patents of possible interest include the following:

Kojima, USP 5,000,188 (1991) (an apparatus for measuring the physiological age of a subject).

Dimri, USP 5,795,728 (1998) ("Biomarkers of cell senescence")

Jia, USP 6,326,209 (2001) ("Measurement and quantification of 17 ketosteroid -sulfates as a biomarker of biological age")

Articles of interest include Kayo, et al., Proc. nat. Acad. Sci. (USA) 98:5093-98 (2001); Han, et al., Mch. Ageing Dev. 115:157-74 (2000); Dozmorov, et al., J. gerontol. A Biol. Sci. Med. Sci. 56:B72-B80 (2001); Dozmorov, et al., Id., 57: B99-B108 (2002); Miller, et al., Mol. Endocrinol., 16: 2657-66 (2002).

### *Apoptosis and CIDE-A*

Apoptosis is a form of programmed cell death that occurs in an active and controlled manner that eliminates unwanted cells. Apoptotic cells undergo an orchestrated cascade of morphological changes such as membrane blebbing, nuclear shrinkage, chromatin condensation, and formation of

apoptotic bodies which then undergo phagocytosis by neighboring cells. One of the hallmarks of cellular apoptosis is the cleavage of chromosomal DNA into discrete oligonucleosomal size fragments. This orderly removal of unwanted cells minimizes the release of cellular components that may affect neighboring tissue. In contrast, membrane rupture and release of cellular components during necrosis often leads to tissue inflammation.

The process of apoptosis is highly conserved and involves the activation of the caspase cascade. Cohen, GM. (1997) Caspases: the executioners of apoptosis. *Biochem. J.* 326:1-16; Budihardjo, I., Oliver, H., Lutter, M., Luo, X., Wang, X. (1999) Biochemical pathways of caspase activation during apoptosis. *Annu. Rev. Cell. Dev.* Biol. 15:269-290; Jacobson, M.D., Weil, M., Raff, M.C. (1997) Programmed cell death in animal development. *Cell* 88:347-354. Caspases are a family of serine proteases that are synthesized as inactive proenzymes. Their activation by apoptotic signals such as CD95 (Fas) death receptor activation or tumor necrosis factor results in the cleavage of specific target proteins and execution of the apoptotic program. Apoptosis may occur by either an extrinsic pathway involving the activation of cell surface death receptors (DR) or by an intrinsic mitochondrial pathway. Yoon, J-H. Gores G.J. (2002) Death receptor-mediated apoptosis and the liver. *J. Hepatology* 37:400-410.

These pathways are not mutually exclusive and some cell types require the activation of both pathways for maximal apoptotic signaling. In type-I cells, death receptor activation leads to the recruitment and activation of caspases-8/10 and the rapid cleavage and activation of caspase-3 in a mitochondrial-independent manner.

Hepatocytes are members of the Type-II cells in which mitochondria are essential for DR-mediated apoptosis. Scaffidi, C., Fulda, S., Srinivasan, A., Friesen, C., Li, F., Tomaselli, K.J., Debatin, K.M., Krammer, P.H., Peter,

M.E. (1998) Two CD95 (APO-1/Fas) signaling pathways. *EMBO J.* 17:1675-1687. In this pathway, the pro-apoptotic protein Bid is truncated activated caspases-8/10 and translocates to the mitochondria. Luo, X., Budihardjo, I., Zou, H., Slaughter, C., Wang, X. (1998) Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. *Cell* 94:481-490; Li, H., Zhu, H., Xu, C.J., Yuan, J. (1998) Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis. *Cell* 94:491-501. This translocation leads to mitochondrial cytochrome c release and eventual activation of caspases-3 and 7 via cleavage by activated caspase-9.

One of the substrates for activated caspase-3 is the DNA fragmentation factor (DFF). DFF is composed of a 45 kDa regulatory subunit (DFF45) and a 40 kDa catalytic subunit (DFF40). Liu, X., Zou, H., Slaughter, C., Wang, X. (1997) DFF, a heterodimeric protein that functions downstream of caspase-3 to trigger DNA fragmentation during apoptosis. *Cell* 89:175-184. DFF45 cleavage by activated caspase-3 results in its dissociation from DFF40 and allows the caspase-activated DNase (CAD) activity of DFF40 to cleave chromosomal DNA into oligonucleosomal size fragments. Liu, X., Li, P., Widlak, P., Zou, H., Luo, X., Garrard, W.T., Wang, X. (1998) The 40-kDa subunit of DNA fragmentation factor induces DNA fragmentation and chromatin condensation during apoptosis. *Proc. Natl. Acad. Sci. USA*. 95:8461-8466; Halenbeck, R., MacDonald, H., Roulston, A., Chen, T.T., Conroy, L., Williams, L.T. (1998) CPAN, a human nucleasé regulated by the caspase-sensitive inhibitor DFF45. *Curr Biol*. 8:537-540; Nagata, S. (2000) Apoptotic DNA fragmentation. *Exp. Cell Res.* 256:12-8.

Recently, a novel family of cell-death-inducing DFF45-like effectors (CIDEs) have been identified that includes CIDE-A, CIDE-B and CIDE-3/FSP2. Inohara, N., Koseki, T., Chen, S., Wu, X., Nunez, G. (1998) CIDE, a novel family of



cell death activators with homology to the 45 kDa subunit of the DNA fragmentation factor. EMBO J. 17:2526-2533; Danesch, U., Hoeck, W., Ringold, G.M. (1992) Cloning and transcriptional regulation of a novel adipocyte-specific gene, FSP27. CAAT-enhancer-binding protein (C/EBP) and C/EBP-like proteins interact with sequences required for differentiation-dependent expression. J. Biol. Chem. 267:7185-7193; Liang, L., Zhao, M., Xu, Z., Yokoyama, K.K., Li, T. (2003) Molecular cloning and characterization of CIDE-3, a novel member of the cell-death-inducing DNA-fragmentation-factor (DFF45)-like effector family. Biochem. J. 370:195-203.

The CIDEs contain an N-terminal domain that shares homology with the N-terminal region of DFF45 and may represent a regulatory region via protein interaction. See Inohara, supra; Lugovskoy, A.A., Zhou, P., Chou, J.J., McCarty, J.S., Li, P., Wagner, G. (1999) Solution structure of the CIDE-N domain of CIDE-B and a model for CIDE-N/CIDE-N interactions in the DNA fragmentation pathway of apoptosis. Cell 9:747-755. The family members also share a C-terminal domain that is necessary and sufficient for inducing cell death and DNA fragmentation; see Inohara supra. The overexpression of CIDE-A induces cell death that can be inhibited by DFF45. However, CIDE-A-induced apoptosis is not inhibited by caspase-8 inhibitors thereby suggesting the presence of additional, caspase-independent, pathway(s) for the induction of apoptosis, see Inohara supra. Previous reports have indicated that human and mouse CIDE-A is expressed in several tissues such as brown adipose tissue (BAT) and heart and is localized to the mitochondria, Zhou, Z., Yon Toh, S., Chen, Z., Guo, K., Ng, C.P., Ponniah, S., Lin, S.C., Hong, W., Li, P. (2003) Cidea-deficient mice have lean phenotype and are resistant to obesity. Nat. Genet. 35:49-56. In addition to the ability to induce apoptosis, CIDE-A can interact and inhibit UCP1 in BAT and may therefore play a role in regulating energy balance, see Zhou supra.

Previous reports have indicated that CIDE-A is not expressed in either adult human or mouse liver tissue, see Inohara supra, Zhou supra. We report here that CIDE-A is not only expressed in adult mouse liver tissue at older ages but is prematurely expressed in hyperinsulinemic and type-II diabetic mouse liver tissue. CIDE-A expression also correlates with liver steatosis in diet-induced obesity, hyperinsulinemia and type-II diabetes. These observations suggest an additional pathway of apoptotic cell death in NAFLD and that CIDE-A may play a role in this serious disease and potentially liver dysfunction associated with type-II diabetes.

## SUMMARY OF THE INVENTION

Our attention recently has focused on the generation of liver mRNA expression profiles and the identification of genes involved in the aging process. We have therefore explored the genetic changes in the liver of C57Bl/6 mice that occur during the aging process, observing the gene expression patterns that occur at many different time points.

Gene chips have been used to identify mouse genes that are differentially expressed in mice, depending upon their age. We have utilized the Amersham product code: 300013 Codelink UniSet Mouse I Bioarray to determine the level of gene expression of approximately 10,000 mouse genes in the liver of mice with average ages of 35, 49, 77, 118, 133, 207, 403, 558 and 725 days.

In essence, complementary RNA derived from mice of different ages was screened for hybridization with oligonucleotide probes each specific to a particular mouse database DNA, as identified, by database accession number, by the gene manufacturer. Each database DNA in turn was also identified by the gene chip manufacturer as representative of a particular mouse gene cluster (Unigene).

In most cases, this database DNA sequence was a full length genomic DNA or cDNA sequence, and are therefore either identical to, or encode the same protein as does, a natural full-length genomic DNA protein coding sequence. Those which don't at least present a partial sequence of a natural gene or its cDNA equivalent.

For the sake of simplicity, all of these mouse database DNA sequences, whether full-length or partial, and whether cDNA or genomic DNA, are referred to herein as "mouse genes". When only the genomic sequence is intended, we will refer specifically to "genomic DNA" or "gDNA".

The sequences in the protein databases are determined either by directly sequencing the protein or, more commonly, by sequencing a DNA, and then determining the translated

amino acid sequence in accordance with the Genetic Code. All of the mouse sequences in the mouse polypeptide database are referred to herein as "mouse proteins" regardless of whether they are in fact full length sequences.

5        Mouse genes which were substantially differentially expressed (younger vs. older), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene, were identified.

10        Favorable behavior is when expression decreases with age. Substantially favorable behavior is when the ratio of younger value to older value is at least two fold. Unfavorable behavior is when expression increases with age. Substantially unfavorable behavior is when the ratio of  
15        older value to younger value is at least two fold.

20        A mouse gene is considered to be "favorable" (more precisely, "wholly favorable") for the purpose of the Master Tables, especially subtable 1A, if, for at least one of the time comparisons set forth in the Examples, it exhibited  
25        substantially favorable behavior, and if, for all the other comparisons, it at least did not exhibit substantially unfavorable behavior. Note that the classification of a gene as favorable for purpose of the Master Table does not mean that it must have exhibited substantially favorable behavior  
30        for all of the comparisons set forth in the Examples.

35        A mouse gene is considered to be "unfavorable" (more precisely, "wholly unfavorable") for the purpose of the Master Tables, especially subtable 1B, if, for at least one of the time comparisons set forth in the Examples, it  
40        exhibited substantially unfavorable behavior, and if, for all the other comparisons, it at least did not exhibit substantially favorable behavior.

45        A mouse gene is considered to be "mixed" (in effect, both partially favorable and partially unfavorable) for the purpose of the Master Tables, especially subtable 1C, if for  
50        at least one of the time comparisons set forth in the

Examples it exhibited substantially favorable behavior and if for at least one of the other such comparisons it exhibited substantially unfavorable behavior.

The expression of a gene may first rise, then fall, with increasing age. Or it may first fall, and then rise. These are just the two simplest of several possible "mixed" expression patterns.

Thus, we can subdivide the "favorables" into wholly and partially favorables. Likewise, we can subdivide the unfavorables into wholly and partially unfavorables. The genes/proteins with "mixed" expression patterns are, by definition, both partially favorable and partially unfavorable. In general, use of the wholly favorable or wholly unfavorable genes/proteins is preferred to use of the partially favorable or partially unfavorable ones.

It is evident from the foregoing that mixed genes/proteins are those exhibiting a combination of favorable and unfavorable behavior. A mixed gene/protein can be used as would a favorable gene/protein if its favorable behavior outweighs the unfavorable. It can be used as would an unfavorable gene/protein if its unfavorable behavior outweighs the favorable. Preferably, they are used in conjunction with other agents that affect their balance of favorable and unfavorable behavior. Use of mixed genes/proteins is, in general, less desirable than use of purely favorable or purely unfavorable genes/proteins.

It will be appreciated that the comparisons set forth in the Examples are not exhaustive and that it is possible that a mouse gene which, on the basis of those comparisons, was classified as a "favorable" gene in the Master Table may turn out, if additional time points are considered, to sometimes exhibit substantially unfavorable behavior. Nonetheless, such a gene will still be considered a "favorable" gene for the purpose of the Master Table and the claims referring to the Master Table. Likewise, a gene which, on the basis of those comparisons, was classified as

an "unfavorable" gene in the Master Table may prove, under more detailed examination, to sometimes exhibit substantially favorable behavior. Nonetheless, it will retain "unfavorable" classification for the purpose of the Master Table and the claims referring thereto.

The "favorable", "unfavorable" and "mixed" mouse proteins are thus those listed in the Master Table as encoded by the listed "favorable", "unfavorable" and "mixed" mouse genes, respectively, or which otherwise correspond to those mouse genes.

Related human genes (database DNAs) and proteins were identified by searching a database comprising human DNAs or proteins for sequences corresponding to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) the mouse gene or protein. The "favorable", "unfavorable" and "mixed" human genes and proteins are those which correspond to the listed "favorable", "unfavorable" and "mixed" mouse genes and proteins, respectively. More than one human protein may be identified as corresponding to a particular mouse chip probe and to a particular mouse gene.

Note that the terms "human genes" and "human proteins" are used in a manner analogous to that already discussed in the case of "mouse genes" and "mouse proteins", e.g., the "genes" include both gDNA and cDNA, and both full and partial sequences.

As used herein, the term "corresponding" does not mean identical, but rather implies the existence of a statistically significant sequence similarity, such as one sufficient to qualify the human protein or gene as a homologous protein or DNA as defined below. The greater the degree of relationship as thus defined (i.e., by the statistical significance of each alignment used to connect the mouse chip DNA, and the corresponding mouse gene/cDNA, to the human protein or gene, measured by an E value), the more close the correspondence. The connection may be direct

25

(mouse gene to human protein) or indirect (e.g., mouse gene to human gene, human gene to human protein). By "mouse gene", we mean the mouse gene from which the gene chip DNA in question was derived.

5 In general, the human genes/proteins which most closely correspond, directly or indirectly, to the mouse genes are preferred, such as the one(s) with the highest, top two highest, top three highest, top four highest, top five highest, and top ten highest E values for the final  
10 alignment in the connection process. The human genes/proteins deemed to correspond to our mouse genes are identified in the Master Tables.

15 Note that it is possible to identify homologous full-length human genes and proteins, if they are present in the database, even if the query mouse DNA or protein sequence is not a full-length sequence.

If there is no homologous full-length human gene or protein in the database, but there is a partial one, the latter may nonetheless be useful. For example, a partial  
20 protein may still have biological activity, and a molecule which binds the partial protein may also bind the full-length protein so as to antagonize a biological activity of the full-length protein. Likewise, a partial human gene may  
25 encode a partial protein which has biological activity, or the gene may be useful in the design of a hybridization probe or in the design of a therapeutic antisense DNA.

The partial genes and protein sequences may of course also be used in the design of probes intended to identify  
30 the full length gene or protein sequence.

Agents which bind the "favorable" and "unfavorable" nucleic acids (e.g., the agent is a substantially  
complementary nucleic acid hybridization probe), or the  
35 corresponding proteins (e.g., an antibody vs. the protein) may be used to estimate the biological age of a human

subject, or to predict the rate of biological aging in a human subject (i.e, to evaluate whether a human subject is at increased or decreased risk for faster-than-normal biological aging.) A subject with one or more elevated  
5 "unfavorable" and/or one or more depressed "favorable" genes/proteins is at increased risk, and one with one or more elevated "favorable" and/or one or more depressed "unfavorable" genes/proteins is at decreased risk.

The assay may be used as a preliminary screening assay  
10 to select subjects for further analysis, or as a formal diagnostic assay.

The identification of the related genes and proteins may also be useful in protecting humans against faster-than-normal or even normal aging (hereinafter, "the disorders").  
15 They may be used to reduce a rate of biological aging in the subject, and/or delay the time of onset, or reduce the severity, of an undesirable age-related phenotype in said subject, and/or protect against an age-related disease.

Thus, Applicants contemplate:

(1) use of the "favorable" mouse DNAs (or fragments thereof) of the Master Tables (below) to isolate or identify  
related human DNAs;

15 (2) use of human DNAs, related to favorable mouse DNAs, to express the corresponding human proteins;

(3) use of the corresponding human proteins (and mouse proteins, if biologically active in humans), to protect  
against the disorder(s);

0 (4) use of the corresponding mouse or human proteins, or nucleic acid probes derived from the mouse or human genes, in diagnostic agents, in assays to measure or predict biological aging or the rate thereof; and

5 (5) use of the corresponding human or mouse genes therapeutically in gene therapy, to protect against the disorder(s).



Moreover Applicants contemplate:

(1) use of the "unfavorable" mouse DNAs (or fragments thereof) of the Master Tables to isolate or identify related human DNAs;

(2) use of the complement to the "unfavorable" mouse DNAs or related human DNAs, as antisense molecules to inhibit expression of the related human DNAs;

(3) use of the mouse or human DNAs to express the corresponding mouse or human proteins;

(4) use of the corresponding mouse or human proteins, in diagnostic agents, to measure biological aging or the rate thereof;

(5) use of the corresponding mouse or human proteins in assays to determine whether a substance binds to (and hence may neutralize) the protein; and

(6) use of the neutralizing substance to protect against the disorder(s).

Thus, DNAs of interest include those which specifically hybridize to the aforementioned mouse or human genes, and are thus of interest as hybridization assay reagents or for antisense therapy. They also include synthetic DNA sequences which encode the same polypeptide as is encoded by the database DNA, and thus are useful for producing the polypeptide in cell culture or in situ (i.e., gene therapy). Moreover, they include DNA sequences which encode polypeptides which are substantially structurally identical or conservatively identical in amino acid sequence to the mouse and human proteins identified in the Master Table 1, subtables 1A or 1C, and DNA sequences which encode human proteins which are members of human protein classes set forth in master table 2, subtables 2A or 2C. Finally, they include DNA sequences which peptide (including antibody) antagonists of the proteins of Master Table 1, subtables 1B or 1C, or of human proteins which are members of human protein classes set forth in master table 2, subtables 2B or

2C.

5

Related human DNAs also may be identified by screening human cDNA or genomic DNA libraries using the mouse gene of the Master Table, or a fragment thereof, as a probe.

10

If the mouse gene of Master Table 1 is not full-length, and there is no closely corresponding full-length mouse gene in the sequence databank, then the mouse DNA may first be used as a hybridization probe to screen a mouse cDNA library to isolate the corresponding full-length sequence.

15

Alternatively, the mouse DNA may be used as a probe to screen a mouse genomic DNA library.

20

The human protein cell death activator CIDE-A is of particular interest because of its highly dramatic change in liver expression with age.

25

The agents of the present invention may be used alone or in conjunction with each other and/or known anti-aging or anti-age-related disease agents. It is of particular interest to use the agents of the present invention in conjunction with an agent disclosed in one of the related applications cited above.

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 CIDE-A Expression is elevated in older normal mice. CIDE-A expression is plotted for normal C57BI/6J mouse ages 35, 49, 56, 77, 133, 207, 403, 558 and 725 days. Expression is low for the first few data points, then rises sharply at 403 days, and again at 558 days. There is a drop off at 725 days, but expression remains above the 403 day level.

Fig. 2 CIDE-A Expression is elevated at an earlier age in diabetic mice. In diabetic mice, the CIDE-A expression at 33 days is more than double that at 77 days, while in normal mice, the increase over the same interval is slight.

Fig. 3. Steatosis in liver of high-fat diet fed mice. Mice were weaned directly onto either a normal diet or a high-fat diet and maintained on the respective diets for up to 26 weeks. The mice were sacrificed and liver tissue isolated. Percent liver white space was determined.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS OF THE  
INVENTION

Full-Length vs. Partial Length Genes/Proteins

5 A "full length" gene is here defined as a (1) a naturally occurring DNA sequence which begins with an initiation codon (almost always the Met codon, ATG), and ends with a stop codon in phase with said initiation codon (if introns, if any, are ignored), and thereby encodes a  
10 naturally occurring polypeptide with biological activity, or a naturally occurring precursor thereof, or (2) a synthetic DNA sequence which encodes the same polypeptide as that which is encoded by (1). The gene may, but need not, include introns.

15 A "full-length" protein is here defined as a naturally occurring protein encoded by a full-length gene, or a protein derived naturally by post-translational modification of such a protein. Thus, it includes mature proteins, proproteins, preproteins and preproproteins. It also  
20 includes substitution and extension mutants of such naturally occurring proteins.

25 **Subjects**

For mice, infancy is defined as the period 0 to 21 days after birth. Sexual maturity is reached, on average, at 42 days after birth. The average lifespan is 832 days.

30 In humans, infancy is defined as the period between birth and two years of age. Sexual maturity in males can occur between 9 and 14 years of age while the average age at first menstrual period for females 15-44 years old is 12.6 years. The average human lifespan is 73 years for males and 79 years for females. The maximum verified human lifespan  
35 was 122 years, five months and 14 days.

### Chronological and Biological Aging

5 "Aging" is a process of gradual and spontaneous change, resulting in maturation through childhood, puberty, and young adulthood and then primarily a decline in function through middle and late age. Aging thus has both the positive component of development/maturation and the negative component of decline.

10 "Senescence" refers strictly to the undesirable changes that occur as a result of post-maturation aging. Some of the changes which occur in post-maturation aging are not deleterious to health (e.g., gray hair, baldness), and some may even be desirable (e.g., increased wisdom and experience). In contrast, the memory impairment that occurs with age is considered senescence. However, we will  
15 hereafter use "aging" per se to refer to "senescence", and use "maturation" to refer to pre-maturation development.

There is increased mortality with age after maturation. There is also a progressive decrease in physiological capacity with age, but the rate of physiological decline  
20 varies from organ to organ and from individual to individual. The physiological decline results in a reduced ability to respond adaptively to environmental stimuli, and increased susceptibility and vulnerability to disease.

"Aging is the accumulation of diverse adverse changes that increase the risk of death. These changes can be attributed to development, genetic defects, the environment, disease, and the inborn aging process. The chance of death at a given age serves as a measure of the number of accumulated changes, that is, of physiologic age, and the  
30 rate of change of this measure, as the rate of aging." Harman, Ann. N.Y. Acad. Sci. 854:1-7 (1998).

Preferably, the agents of the present invention inhibit aging for at least a subpopulation of mature (post-puberty) adult subjects.

5 The term "healthy aging" (sometimes called "successful aging") refers to post-maturation changes in the body that

occur with increasing age even in the absence of an overt disease. However, increased age is a risk factor for many diseases ("age-related diseases"), and hence "total aging" includes both the basal effects of healthy aging and the effects of any age-related disease. (Most literature uses the term "normal aging" as a synonym for "healthy aging", but a minority use it to refer to "total aging". To minimize confusion, we will try to avoid the term "normal aging", but if we use it, it is as a synonym for "healthy aging".) Some scientists have suggested that normal aging changes should be defined as those which are universal, degenerative, progressive and intrinsic.

Preferably, the agents of the present invention inhibit healthy aging for at least a subpopulation of mature (post-puberty) adult subjects.

In both aging and senescence, many physiologic functions decline, but normal decline is not usually considered the same as disease. The distinction between normal decline and disease is often but not always clear and may be due only to statistical distribution. Glucose intolerance is considered consistent with healthy aging, but diabetes is considered a disease, although a very common one. Cognitive decline is nearly universal with advanced age and is considered healthy aging; however, cognitive decline consistent with dementia, although common in late life, is considered a disease (as in the case of Alzheimer's, a conclusion supported by analysis of brain tissue at autopsy). A decline in maximal heart rate is typical of healthy aging. In contrast, coronary heart disease is an age-related disease. A decline in bone density is considered healthy aging, but when it drops to 2.5 SD below the young adult mean, it is called osteoporosis. Generally speaking, the changes typical of healthy aging are gradual, while those typical of a disorder can be rapid.

The term average (median) "lifespan" is the chronological age to which 50% of a given population

survive. The maximum lifespan potential is the maximum age achievable by a member of the population. As a practical matter, it is estimated as the age reached by the longest lived member (or former member) of the population. The (average) life expectancy is the number of remaining years that an individual of a given age can expect to live, based on the average remaining lifespans of a group of matched individuals.

The most widely accepted method of measuring the rate of aging is by reference to the average or the maximum lifespan. If a drug treatment achieves a statistically significant improvement in average or maximum lifespan in the treatment group over the control group, then it is inferred that the rate of aging was retarded in the treatment group. Similarly, one can compare long-term survival between the two groups.

Preferably, the agents of the present invention have the effect of increasing the average lifespan and/or the maximum lifespan for at least a subpopulation of mature (post-puberty) adult subjects. This subpopulation may be defined by sex and/or age. If defined in part by age, then it may be defined by a minimum age (e.g., at least 30, at least 40, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 90, etc.) or by a maximum age (not more than 40, not more than 50, not more than 55, not more than 60, not more than 65, not more than 70, not more than 75, not more than 80, not more than 90, not more than 100, etc.), or by a rational combination of a minimum age and a maximum age so as to define a preferred close-ended age range, e.g., 55-75.

The subpopulation may additionally be defined by race, e.g., caucasian, negroid or oriental, and/or by ethnic group, and/or by place of residence (e.g., North America, Europe).

The subpopulation may additionally be defined by non-age risk factors for age-associated diseases, e.g., by blood

pressure, body mass index, etc.

Preferably, the subpopulation in which an agent of the present invention is reasonably expected to be effective is large, e.g., in the United States, preferably at least 100,000 individuals, more preferably at least 1,000,000 individuals, still more preferably at least 10,000,000, even more preferably at least 20,000,000, most preferably at least 40,000,000.

By way of comparison, according to the 2000 U.S. Census, the U.S. population, by age, was

Age	Pop (mil)
15-19	20.2
20-24	19.0
25-29	19.4
30-34	20.5
35-39	22.7
40-44	22.4
45-49	20.1
50-54	17.6
55-59	13.5
60-64	10.8
65-69	9.5
70-74	8.9
75-79	7.4
80-84	4.9
85+	4.2

For any given chronological age, statisticians can define the probability of living to a particular later age. These expectancies can be calculated for the entire age cohort, or broken down by sex, race, country of residence, etc. Individuals who live longer than expected can be said, after the fact, to have biologically aged more slowly



than their peers. One definition of biological age is that it is a measure of one's position in one's life span, i.e., biological age = position in own life span (as fraction in range 0..1) X average life span for species. This simple definition carries with it the implicit assumption that the rate of biological aging is constant. It also has the practical problem of determining one's own life span before death. We will present a more practical definition shortly.

The problem with lifespan studies is that they are extremely time-consuming. A maximum lifespan study in mice can take 4-5 years. A maximum lifespan study in dogs or cats would take 15-20 years, in monkeys, 30-40 years, and in humans, over 100 years. Even if the human study group were of sexagenarians, it would take 40-60 years to complete the study.

Hence, scientists have sought to identify biological markers (biomarkers) of biological aging, that is, characteristics that can be measured while the subjects are still alive, which correlate to lifespan. These biological markers can be used to calculate a "biological age" (syn. "Physiological age"); it is the chronological age at which an average member of the population (or relevant subpopulation) would have the same value of a biomarker of biological aging (or the same value of a composite measure of biomarkers of biological aging) as does the subject. This is the definition that will be used in this disclosure, unless otherwise stated.

The effect of aging varies from system to system, organ to organ, etc. For example, between ages 30 and 70 years, nerve conduction velocity decreases by only about 10%, but renal function decreases on average by nearly 40%. Thus, there isn't just one biological age for a subject. By a suitable choice of biomarker, one may obtain a whole organism, or a system-, organ- or tissue-specific measure of biological aging, e.g., one can say that a person has the nervous system of a 30 year old but the renal system of a 60

year old. Biomarkers may measure changes at the molecular, cellular, tissue, organ, system or whole organism levels.

Generally speaking, in the absence of some form of intervention (drugs, diet, exercise, etc.), biological ages will increase with time. The agents of the present invention preferably reduce the time rate of change of a biological age of the subject. The term "a biological age" could refer to the overall biological age of the subject, to the biological age of a particular system, organ or tissue of that subject, or to some combination of the foregoing. More preferably, the agents of the present cannot only reduce the rate of increase of a biological age of the subject, but can actually reduce a biological age of the subject.

A simple biologic marker (biomarker) is a single biochemical, cellular, structural or functional indicator of an event in a biologic system or sample. A composite biomarker is a mathematical combination of two or more simple biomarkers. (Chronological age may be one of the components of a composite biomarker.)

A plausible biomarker of biological age would be a biomarker which shows a cross-sectional and/or longitudinal correlation with chronological age. Nakamura suggests that it is desirable that a biomarker show (a) significant cross-sectional correlation with chronological age, (b) significant longitudinal change in the same direction as the cross-sectional correlation, (c) significant stability of individual differences, and (d) rate of age-related change proportional to differences in life span among related species. Cp. Nakamura, Exp Gerontol. 29(2):151-77 (1994), using desiderata (a)-(c). A superior biomarker of biological age would be a better predictor of lifespan than is chronological age (preferably for a chronological age at which 90% of the population is still alive).

The biomarker preferably also satisfies one or more of

the following desiderata: a statistically significant age-related change is apparent in humans after a period of at most a few years; not affected dramatically by physical conditioning (e.g., exercise), diet, and drug therapy (unless it is possible to discount these confounding influences, e.g., by reference to a second marker which measures them); can be tested repeatedly without harming the subject; works in lab animals as well as humans; simple and inexpensive to use; does not alter the result of subsequent tests for other biomarkers if it is to be used in conjunction with them; monitors a basic process that underlies the aging process, not the effects of disease.

Preferably, if the biomarker works in lab animals, there is a statistically significant difference in the value of the biomarker between groups of food-restricted and normally-fed animals. It has been shown in some mammalian species that dietary restriction without malnutrition (e.g., caloric decrease of up to 40% from ad libitum feeding) increases lifespan.

A biomarker of aging may be used to predict, instead of lifespan, the "Healthy Active Life Expectancy" (HALE) or the "Quality Adjusted Life Years" (QALY), or a similar measure which takes into account the quality of life before death as well as the time of death itself. For HALE, see Jagger, in *Outcomes Assessment for Healthcare in Elderly People*, 67-76 (Farrand Press: 1997). For QALY, see Rosser RM. A health index and output measure, in Stewart SR and Rosser RM (eds) *Quality of Life: Assessment and Application*. Lancaster: MTP, 1988.

A biomarker of aging may be used to predict, instead of lifespan, the timing and/or severity of a change in one or more age-related phenotypes as described below.

A biomarker of aging may be used to estimate, rather than overall biological age for a subject, a biological age for a specific body system or organ. The determination of the biological age of the liver, and the inhibition of

biological aging of the liver, are of particular interest.

Body systems include the nervous system (including the brain, the sensory organs, and the sense receptors of the skin), the cardiovascular system (includes the heart, the red blood cells and the reticuloendothelial system), the respiratory system, the gastrointestinal system, the endocrine system (pituitary, thyroid, parathyroid and adrenal glands, gonads, pancreas, and paranglia), the musculoskeletal system, the urinary system (kidneys, bladder, ureters, urethra), the reproductive system and the immune system (bone marrow, thymus, lymph nodes, spleen, lymphoid tissue, white blood cells, and immunoglobulins). A biomarker may be useful in estimating the biological age of a system because the biomarker is a chemical produced by that system, because it is a chemical whose activity is primarily exerted within that system, because it is indicative of the morphological character or functional activity of that system, etc. A given biomarker may be thus associated with more than one system. In a like manner, a biomarker may be associated with the biological age, and hence the state, of a particular organ or tissue.

The prediction of lifespan, or of duration of system or organ function at or above a particular desired level, may require knowledge of the value of at least one biomarker of aging at two or more times, adequately spaced, rather than of the value at a single time. See McClearn, Biomarkers of Age and Aging, Exp. Gerontol., 32:87-94 (1997).

The levels (or changes in levels) of the human proteins identified in this specification, and their corresponding mRNAs, may be used as simple biomarkers (direct or inverse) of biological aging. They may be used in conjunction with each other, or other simple biomarkers, in a composite biomarker.

Once several plausible simple biomarkers have been

identified, a composite biomarker may be obtained by standard mathematical techniques, such as multiple regression, principal component analysis, cluster analysis, neural net analysis, and so forth. As a preliminary to such analysis, the values may be standardized, e.g., by converting the raw scores into z-scores based on the distributions for each simple biomarker.

For example, principal component analysis can be used to analyze the variation of lifespan with different observables, and the factor score coefficients from the first principal component can be used to derive an equation for estimating a biological age score. Nakamura, Exp Gerontol. 29(2):151-77 (1994). This approach was used to obtain the following BAS (for healthy Japanese women aged 28-80):  $BAS = -4.37 - 0.998FEV_{1.0} + 0.022SBP + 0.133MCH + 0.018GLU - 1.505 A/G \text{ RATIO}$ , where  $FEV_{1.0}$  is the forced expiratory volume in 1 sec. (Liters), SBP is the systolic blood pressure (mm Hg), MCH is the mean corpuscular hemoglobin (pg), GLU is glucose (mg/dl), and A/G RATIO is the ratio of albumin to globulin. The relative importance of these five biomarkers was 33.7%, 25.1%, 17.1%, 14.8% and 8.9%, respectively. Ueno, et al., "Biomarkers of Aging in Women and the Rate of Longitudinal Changes," J. Physiol. Anthropol. 22(1): 37-46 (Jan. 2003).

It should be noted that particularly when evaluating the overall biological age of the subject, it is not necessarily most desirable to weight all systems or all organs equally. One may find it more desirable to give greater weight to the system or organ with the highest biological age in calculating the overall biological age, because it is presumably more likely to deteriorate or fail, resulting in death. Appropriate statistical analysis can be used to find the weighting scheme resulting in the best prediction of lifespan.

In the H-SCAN (Hoch Company) test, a composite of 12

simple biomarkers is used to measure human aging:

#### SENSORY

1. Highest audible pitch (kHz)
2. Visual accommodation (diopters)
3. Vibrotactile sensitivity (dB)

#### MOTOR

4. Muscle Movement time (sec)
5. Muscle Movement time with decision (sec)
6. Alternate button tapping time (sec)

#### COGNITIVE

7. Memory, length of sequence
8. Auditory reaction time (sec)
9. Visual reaction time (sec)
10. Visual Reaction time with decision (sec)

#### PULMONARY

11. Forced vital capacity (liters)
12. Forced expiratory Volume- 1 sec (liters)

See Hochschild, R., Journal of Gerontology [Biological Science] 45(6):B187-214; 1990).

According to a website discussing the H-SCAN test, "Biomarkers of aging are characteristics of an organism that correlate in large groups with chronological age and mortality. Of particular value in human applications are biomarkers of aging that also correlate with the quality of life in later life in the sense that they involve functions that are crucial to carrying out the activities of daily living.... A single biomarker of aging is limited by the fact that it measures only one isolated characteristic and is hardly representative of the diversity of functional and structural concomitants of aging.... Biological age, in

contrast to chronological age, is an individual's hypothetical age calculated from scores obtained on a battery of tests of biomarkers of aging. As a first step in the calculation, the age of which each biomarker score is typical is determined by comparison with scores obtained by a large representative group of persons (or organisms) spanning a range of ages. Then one of a variety of averaging techniques is employed (optionally with standardization steps) to obtain a single index of age, as described in detail by Hochschild. This index varies with, and therefore must be expressed with reference to, the measured biomarkers and the mathematical method of combining scores."

<http://www.longevityinstituteone.com/>

Abbo, USP 6,547,729 teaches determining the biological age (he calls it "performance age") of a subject by (1) for a sample population, determining a regression curve relating some set of observed values for an "indicator" of the functionality of a bodily system to the chronological age of the observed individuals, (2) solving the regression equation to obtain a predicted performance age, given the value of the indicator for the subject. The regression can be based on more than one indicator, i.e., it can be a multiple regression. The sample population can be defined by sex, age range, ethnic composition, and geographic location. The bodily system may be a molecular, cellular, tissue or organ system. The following indicators are suggested by Abbo: nervous system (memory tests, reaction time, serial key tapping, digit recall test, letter fluency, category fluency, nerve conduction velocity), arteries (pulse wave velocity; ankle-brachial index), skeletal system (bone mineral density); lungs (forced vital capacity), heart (ejection fraction; length of time completed on a treadmill stress test), kidneys (creatinine clearance), proteins (glycosylation of hemoglobin), endocrine glands (load level of bioactive testosterone; level of dehydroepiandrosterone

sulfate, ratio of urinary 17-ketosteroids/17-hydroxycorticosteroids; growth hormone; IGF-1).

Preferably, the agents of the invention have a favorable effect on the value of at least one simple biomarker of biological aging, such as any of the plausible biomarkers mentioned anywhere in this specification, other than the level of one of the proteins of the present invention. More preferably, they have a favorable effect on the value of at least two such simple biomarkers of biological aging. Even more preferably, at least one such pair is of markers which are substantially non-correlated ( $R^2 < 0.5$ ).

Desirably, if more than one simple biomarker is favorably affected, the biomarkers in question reflect different levels of organization, and/or different body components at the same level of organization. For example, a visual reaction time with decision test is on the whole organism level, while a measurement of telomere length is on the cellular level.

A biomarker may, but need not, be an indicator related to one of the postulated causes or contributing factors of aging. It may, but need not, be an indicator of the acute health of a particular body system or organ.

A biomarker may measure behavior, cognitive or sensory function, or motor activity, or some combination thereof. It may measure the level of a type of cell (e.g., a T cell subset, such as CD4, CD4 memory, CD4 naive, and CD4 cells expressing P-glycoprotein) or of a particular molecule (e.g., growth hormone, IGF-1, insulin, DHEAS, an elongation factor, melatonin) or family of structurally or functionally related molecules in a particular body fluid (especially blood) or tissue. For example, lower serum IGF-1 levels are correlated with increasing age, and IGF-1 is produced by



many different tissues. On the other hand, growth hormone is produced by the pituitary gland.

A biomarker may measure an indicator of stress (particularly oxidative stress) and resistance thereto. It has been theorized that free radicals damage biomolecules, leading to aging.

A biomarker may measure protein glycation or other protein modification (e.g., collagen crosslinking). It has been theorized that such modifications contribute to aging.

The biomarker may measure changes in the lengths of telomeres or in the rate of cell division. It has been theorized that telomere shortening beyond a critical length leads the cell to stop proliferating. Average telomere length therefore provides a biomarker as to how many divisions the cell as previously undergone and how many divisions the cell can undergo in the future.

Suggested biomarkers have also included resting heart rate, resting blood pressure, exercise heart rate, percent body fat, flexibility, grip strength, push strength, abdominal strength, body temperature, and skin temperature.

The present invention does not require that all of the biomarkers identified above be validated as indicative of biological age, or that they be equally useful as measures of biological age.

There is an overlap between biomarkers of aging and indicators of functional status. An indicator of functional status is an indicator that defines a functional ability (e.g., physiological, cognitive or physical function). An indicator of functional status may also be related to the increase in morbidity and mortality with chronological age. Such indicators preferably predict physiological, cognitive and physical function in an age-coherent way, and do so better than chronological age. Preferably, they can predict the years of remaining functionality, and the trajectory toward organ-specific illness in the individual. Also, they

are preferably minimally invasive.

Suggested indicators include anthropometric data (body mass index, body composition, bone density, etc.), functional challenge tests (glucose tolerance, forced vital capacity), physiological tests (cholesterol/HDL, glycosylated hemoglobin, homocysteine, etc.) and proteomic tests.

A number of mouse models for human aging exist. See Troen, supra, Table 3. The drugs identified by the present invention may be further screened in one or more of these models.

#### Age-Related Phenotype

An age-related phenotype is an observable change which occurs with age. An age-related phenotype may, but need not, also be a biomarker of biological aging.

Preferably, the agent of the present invention favorably affects at least one age-related phenotype. More preferably, it favorably affects at least two age-related phenotypes, more preferably phenotypes of at least two different body systems.

The age-related phenotype may be a system level phenotype, such as a measure of the condition of the nervous system, respiratory system, immune system, circulatory system, endocrine system, reproductive system, gastrointestinal system, or musculoskeletal system.

The age-related phenotype may be an organ level phenotype, such as a measure of the condition of the brain, eyes, ears, lungs, spleen, heart, pancreas, liver, ovaries, testicles, thyroid, prostate, stomach, intestines, or kidney.

45

The age-related phenotype may be a tissue level phenotype, such as a measure of the condition of the muscle, skin, connective tissue, nerves, or bones.

- 5 The age-related phenotype may be a cellular level phenotype, such as a measure of the condition of the cell wall, mitochondria or chromosomes.

- The age-related phenotype may be a molecular level  
phenotype, such as a measure of the condition of nucleic  
acids, lipids, proteins, oxidants, and anti-oxidants.

- The age-related phenotype may be manifested in a biological  
fluid, such as blood, urine, saliva, lymphatic fluid or  
cerebrospinal fluid. The biochemical composition of these  
fluid may be an overall, system level, organ level, tissue  
level, etc. phenotype, depending on the specific biochemical  
and fluid involved.

#### PHYSIOLOGICAL AGING OF THE HUMAN BODY BY SYSTEMS

SKIN, HAIR, NAILS	Loss of subcutaneous fat, Thinning of skin, Decreased collagen, Nails brittle and flake, Mucous membranes drier, Less sweat glands, Temperature regulation difficult, Hair pigment decreases, Hair thins. Eyelids baggy and wrinkled.
----------------------	--

EYES AND VISION	<p>Eyes deeper in sockets; Conjunctiva thinner and yellow; Quantity of tears decreases; Iris fades; Pupils smaller, let in less light; Night and depth vision less; "Floaters" can appear</p> <p>Lens enlarges; Lens becomes less transparent, can actually become clouded, results in cataracts; Accommodation decreases, results in presbyopia; Impaired color vision, also - especially greens and blues-- because cones degenerate; Predisposed to glaucoma (Increased pressure in eye, decreased absorption of intraocular fluid; can result in blindness);</p> <p>Macular degeneration becoming more frequent (This is the patch of retina where lens focuses light, Ultimately results in blindness )</p>
EARS AND HEARING LOSS	<p>Irreversible, sensorineural loss (presbycusis) with age (Men more affected than women, Loss occurs in higher range of sound, By 60 years, most adults have trouble hearing above 4000Hz, Normal speech 500-2000Hz)</p>
RESPIRATORY SYSTEM	<p>Lungs become more rigid, Pulmonary function decreases, Number and size of alveoli decreases, Vital capacity declines, Reduction in respiratory fluid, Bony changes in chest cavity</p>
CARDIOVASCUL AR SYSTEM	<p>Heart smaller and less elastic with age, By age 70 cardiac output reduced 70%, Heart valves become sclerotic, Heart muscle more irritable, More arrhythmias, Arteries more rigid, Veins dilate</p>

GASTROINTESTINAL SYSTEM	Reduced GI secretions, Reduced GI motility, Decreased weight of liver, Reduced regenerative capacity of liver, Liver metabolizes less efficiently
RENAL SYSTEM	After 40 renal function decreases, By 90 lose 50% of function, Filtration and reabsorption reduced, Size and number of nephrons decrease, Bladder muscles weaken, Less able to clear drugs from system, Smaller kidneys and bladder
5 REPRODUCTIVE SYSTEM (MALE)	Reduced testosterone level, Testes atrophy and soften, Decrease in sperm production, Seminal fluid decreases and more viscous, Erections take more time, Refractory period after ejaculation may lengthen to days
REPRODUCTIVE SYSTEM (FEMALE)	Declining estrogen and progesterone levels, Ovulation ceases, Introitus constricts and loses elasticity, Vagina atrophies - shorter and drier, Uterus shrinks, Breasts pendulous and lose elasticity
10 NEUROLOGICAL SYSTEM	Neurons of central and peripheral nervous system degenerate, Nerve transmission slows, Hypothalamus less effective in regulating body temperature, Reduced REM sleep, decreased deep sleep, After age 50, lose 1% of neurons each year
MUSCULOSKELETAL SYSTEM	Adipose tissue increases with age, Lean body mass decreases, Bone mineral content diminished, Decrease in height from narrow vertebral spaces, Less resilient connective tissue, Synovial fluid more viscous, May have exaggerated curvature of spine

IMMUNE SYSTEM	Decline in immune function, Trouble differentiating between self and non-self - more auto-immune problems, Decreases antibody response, Fatty marrow replaced red marrow, Vitamin B12 absorption might decrease - decreased hemoglobin and hematocrit
ENDOCRINE SYSTEM	Decreased ability to tolerate stress - best seen in glucose metabolism, Estrogen levels decrease in women, Other hormonal decreases include testosterone, aldosterone, cortisol, progesterone

Adapted from [http://www.texasstate.com/html/ger\\_pap1.ppt](http://www.texasstate.com/html/ger_pap1.ppt)

The aging human liver appears to preserve its morphology and function relatively well. The liver appears to progressively decrease in both mass and volume. It also appears browner (a condition called "brown atrophy"), as a result of accumulation of lipofuscin (ceroid) within hepatocytes. Increases occur in the number of macrohepatocytes, and in polyploidy, especially around the terminal hepatic veins. The number of mitochondria declines, and both the rough and smooth endoplasmic reticulum diminish. The number of lysozymes increase.

The liver is the premiere metabolic organ of the body. With regard to metabolism, hepatic glycerides and cholesterol levels increase with age, at least up to age 90. On the other hand, phospholipids, aminotransferases, and serum bilirubin appear to remain normal. There are contradictory reports as to the effect of aging on albumin, serum gamma-glutamyltransferase, and hepatic alkaline phosphatase. It is worth noting that it has been shown that the content of cytochrome oxidase exhibits a progressive decline which correlates with age-associated decline in mtRNA synthesis in brain, liver, heart, lungs and skeletal

muscle.

See generally Anantharaju, Feller and Chedid, "Aging Liver: A Review," Gerontology, 48: 343-53 (2002).

## 5    Quality of Life

Clinicians are interested, not only in simple prolongation of lifespan, but also in maintenance of a high quality of life (QOL) over as much as possible of that lifespan. QOL can be defined subjectively in terms of the subject's

10   satisfaction with life, or objectively in terms of the subject's physical and mental ability (but not necessarily willingness) to engage in "valued activities", such as those which are pleasurable or financially rewarding.

15   Flanagan has defined five domains of QOL, capturing 15 dimensions of life quality. The five domains, and their component dimensions, are physical and material well being (Material well-being and financial security; Health and personal safety), Relations with other people (relations

20   with spouse; Having and rearing children; Relations with parents, siblings, or other relatives ; Relations with friends) Social, community, civic activities (Helping and encouraging others; Participating in local and governmental affairs ), Personal

25   development, fulfillment (Intellectual development; Understanding and planning; Occupational role career; Creativity and personal expression), and recreation (Socializing with others; Passive and observational recreational activities; Participating in active

30   recreation). See Flanagan JC, . "A research approach to improving our quality of life." Am Psychol 33:138-147 (1978).

"Health-related quality of life" (HRQL or HRQOL) is an

35   individual's satisfaction or happiness with domains of life insofar as they affect or are affected by "health".

50

In a preferred embodiment, a pharmaceutical agent of the present invention is able to achieve a statistically significant improvement in the expected quality of life, measured according to a commonly accepted measure of QOL, in a treatment group over a control group.

While there is general acceptance of the notion that QOL is important, quantifying QOL is not especially straightforward. Also, QOL can only be measured in humans. Measurements of QOL can be objective (e.g., employment status, marital status, home ownership) or subjective (the subject's opinion of his or her life), or some combination of the two.

A simple approach to measuring subjective QOL is to simply have the subjects rate their overall quality of life on a scale, e.g., of 7 points. One can also use more elaborate measure, such as the Older Adult Health and Mood Questionnaire (a 22 item test for assessing depression). Objective QOL can be measured by, e.g., an activities checklist.

There is a relationship between QOL assessment and so-called ADL or IADL measures, which assess the need for assistance.

The Katz Index of Independence in Activities of Daily Living (Katz ADL) measures adequacy of independent performance of bathing, dressing, toileting, transferring, continence, and feeding. See Katz, S., "Assessing Self-Maintenance: Activities of Daily Living, Mobility and Instrumental Activities of Daily Living, Journal of the American Geriatrics Society, 31(12); 721-726 (1983); Katz S., Down, T.D., Cash, H.R. et al. Progress in the Development of the Index of ADL. Gerontologist, 10: 20-30 (1970).

Performance of a more sophisticated nature is measured by



the "Instrumental Activities of Daily Living" (IADL) scale. This inquires into ability to independently use the telephone, shop, prepare food, carry out housekeeping, do laundry, travel locally, take medication and handle finances. See Lawton, MP and Brody, EM, Gerontologist, 9:179-86 (1969).

The 36 question Medical Outcomes Study Short Form (SF-36) (Medical Outcomes Trust, Inc., 20 Park Plaza, Suite 1014, Boston, Massachusetts 02116) assesses eight health concepts: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions.

A low score on an ADL, IADL or SF-36 test is likely to be associated with a low QOL, but a high score does not guarantee a high QOL because these tests do not explore performance of "valued activities", only of more basic activities. Nonetheless, these tests can be considered commonly accepted measures of QOL for the purpose of this invention.

#### Age-Related Diseases

Age-related (senescent) diseases include certain cancers, atherosclerosis, diabetes (type 2), osteoporosis, hypertension, depression, Alzheimer's, Parkinson's, glaucoma, certain immune system defects, kidney failure, and liver steatosis. In general, they are diseases for which the relative risk (comparing a subpopulation over age 55 to a suitably matched population under age 55) is at least 1.1.

Preferably, the agents of the present invention protect

against one or more age-related diseases for at least a subpopulation of mature (post-puberty) adult subjects.

### *Diabetes*

Type II diabetes is of particular interest. A deficiency of insulin in the body results in diabetes mellitus, which affects about 18 million individuals in the United States. It is characterized by a high blood glucose (sugar) level and glucose spilling into the urine due to a deficiency of insulin. As more glucose concentrates in the urine, more water is excreted, resulting in extreme thirst, rapid weight loss, drowsiness, fatigue, and possibly dehydration. Because the cells of the diabetic cannot use glucose for fuel, the body uses stored protein and fat for energy, which leads to a buildup of acid (acidosis) in the blood. If this condition is prolonged, the person can fall into a diabetic coma, characterized by deep labored breathing and fruity-odored breath.

There are two types of diabetes mellitus, Type I and Type II. Type II diabetes is the predominant form found in the Western world; fewer than 8% of diabetic Americans have the type I disease.

*Type I diabetes.* In Type I diabetes, formerly called juvenile-onset or insulin-dependent diabetes mellitus, the pancreas cannot produce insulin. People with Type I diabetes must have daily insulin injections. But they need to avoid taking too much insulin because that can lead to insulin shock, which begins with a mild hunger. This is quickly followed by sweating, shallow breathing, dizziness, palpitations, trembling, and mental confusion. As the blood sugar falls, the body tries to compensate by breaking down fat and protein to make more sugar. Eventually, low blood sugar leads to a decrease in the sugar supply to the brain, resulting in a loss of consciousness. Eating a sugary food can prevent insulin shock until appropriate medical measures

can be taken.

Type I diabetics are often characterized by their low or absent levels of circulating endogenous insulin, i.e., hypoinsulinemia (1). Islet cell antibodies causing damage to the pancreas are frequently present at diagnosis. Injection of exogenous insulin is required to prevent ketosis and sustain life.

*Type II diabetes.* Type II diabetes, formerly called adult-onset or non-insulin-dependent diabetes mellitus (NIDDM), can occur at any age. The pancreas can produce insulin, but the cells do not respond to it.

Type II diabetes is a metabolic disorder that affects approximately 17 million Americans. It is estimated that another 10 million individuals are "prone" to becoming diabetic. These vulnerable individuals can become resistant to insulin, a pancreatic hormone that signals glucose (blood sugar) uptake by fat and muscle. In order to maintain normal glucose levels, the islet cells of the pancreas produce more insulin, resulting in a condition called hyperinsulinemia. When the pancreas can no longer produce enough insulin to compensate for the insulin resistance, and thereby maintain normal glucose levels, hyperglycemia (elevated blood glucose) results, and type II diabetes is diagnosed.

Early Type II diabetics are often characterized by hyperinsulinemia and resistance to insulin. Late Type II diabetics may be normoinsulinemic or hypoinsulinemic. Type II diabetics are usually not insulin dependent or prone to ketosis under normal circumstances.

Little is known about the disease progression from the normoinsulinemic state to the hyperinsulinemic state, and from the hyperinsulinemic state to the Type II diabetic state.

As stated above, type II diabetes is a metabolic disorder that is characterized by insulin resistance and

impaired glucose-stimulated insulin secretion (2,3,4). However, Type II diabetes and atherosclerotic disease are viewed as consequences of having the insulin resistance syndrome (IRS) for many years (5). The current theory of the pathogenesis of Type II diabetes is often referred to as the "insulin resistance/islet cell exhaustion" theory. According to this theory, a condition causing insulin resistance compels the pancreatic islet cells to hypersecrete insulin in order to maintain glucose homeostasis. However, after many years of hypersecretion, the islet cells eventually fail and the symptoms of clinical diabetes are manifested. Therefore, this theory implies that, at some point, peripheral hyperinsulinemia will be an antecedent of Type II diabetes. Peripheral hyperinsulinemia can be viewed as the difference between what is produced by the beta cell minus that which is taken up by the liver. Therefore, peripheral hyperinsulinemia can be caused by increased  $\beta$  cell production, decreased hepatic uptake or some combination of both. It is also important to note that it is not possible to determine the origin of insulin resistance once it is established since the onset of peripheral hyperinsulinemia leads to a condition of global insulin resistance.

Multiple environmental and genetic factors are involved in the development of insulin resistance, hyperinsulinemia and type II diabetes. An important risk factor for the development of insulin resistance, hyperinsulinemia and type II diabetes is obesity, particularly visceral obesity (6,7,8). Type II diabetes exists world-wide, but in developed societies, the prevalence has risen as the average age of the population increases and the average individual becomes more obese.

#### Role of the Liver in the Development of Diabetes

Insulin stimulates the liver to store glucose in the

form of glycogen. A large fraction of glucose absorbed from the small intestine is immediately taken up by hepatocytes, which convert it into the storage polymer glycogen. Hepatic uptake of insulin is a function of the number and efficiency of the liver's insulin receptors, and the factors which affect them are not well understood.

In the liver, insulin activates the enzyme hexokinase, which phosphorylates glucose, trapping it within the cell. Insulin also activates several of the enzymes that are directly involved in glycogen synthesis, including phosphofructokinase and glycogen synthase. However, insulin also acts to inhibit the activity of glucose-6-phosphatase.

When the liver is saturated with glycogen, any additional glucose taken up by hepatocytes is shunted into pathways leading to synthesis of fatty acids, which are exported from the liver as lipoproteins. The lipoproteins are ripped apart in the circulation, providing free fatty acids for use in other tissues, including adipocytes, which use them to synthesize triglyceride.

In the absence of insulin, glycogen synthesis in the liver ceases and enzymes responsible for breakdown of glycogen become active.

As noted above, peripheral hyperinsulinemia can be viewed as the difference between what insulin is produced by the  $\beta$  cell minus that which is taken up by the liver. Therefore, peripheral hyperinsulinemia can be caused by increased  $\beta$  cell production, decreased hepatic uptake or some combination of both.

#### Effect of Diabetes on the Liver

Diabetes is associated with nonalcoholic steatohepatitis (NASH), also known as nonalcoholic fatty liver disease (NAFLD). In NASH, fat builds up in the liver and eventually causes scar tissue (cirrhosis of the liver).

Non-alcoholic fatty liver disease (NAFLD) is now recognized as one of the most common causes of liver disease

and is estimated to affect 10 to 24% of the general population. The higher prevalence of NAFLD in persons with obesity, hyperinsulinemia or type-II diabetes suggests that diet and insulin resistance may play a pivotal role in the development of this syndrome. NAFLD is a clinicopathologic syndrome with a wide spectrum of liver damage ranging from simple steatosis to steatohepatitis (NASH) to advanced fibrosis and cirrhosis. Hepatic steatosis is caused by lipid accumulation within hepatocytes and is a relatively benign condition. However steatosis combined with necro-inflammatory activity may progress to end-stage liver disease. It appears that the disease progression requires cellular injury and inflammation in a steatotic environment. While the cause of the injury is not understood, it is clear that hepatic apoptosis is a prominent feature of non-alcoholic steatosis as well as other liver diseases. See generally Alba, L.M., Lindor, K. (2003) Review article: Non-alcoholic fatty liver disease., *Aliment Pharmacol. Ther.* 17:977-986; Ludwig, J., Viggiano, T.R., McGill, D.B., Oh, B.J. (1980) Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin. Proc.* 55:434-438; Chitturi, S., Abeygunasekera, S., Farrell, G.C., Holmes-Walker, J., Hui, J.M., Fung, C., Karim, R., Lin, R., Samarasinghe, D., Liddle, C., Weltman, M., George, J. (2002) NASH and insulin resistance: Insulin hypersecretion and specific association with the insulin resistance syndrome. *Hepatology* 35:373-379; Feldstein, A.E., Canbay, A., Angulo, P., Taniai, M., Burgart, L.J., Lindor, K.D., Gores, G.J. (2003) Hepatocyte apoptosis and fas expression are prominent features of human nonalcoholic steatohepatitis. *Gastroenterology* 125:437-443; Higuchi, H., Gores, G.J. (2003) Mechanisms of liver injury: an overview. *Curr. Mol. Med.* 3:483-490.

Drugs used for the treatment of diabetes, such as Rezulin (troglitazone), can cause liver damage.

### Diseases Characterized by Accelerated Aging

Several human diseases display some features of accelerated aging. These include Werner's syndrome (classic early-onset progeria), Hutchinson-Gilford syndrome (adult progeria), and Down's syndrome (trisomy 21). Troen, *Biology of Aging, Mt. Sinai J. Med.*, 70(1): 3 (Jan. 2003). Thus, the present invention may be useful in the treatment (curative or ameliorative) of individuals with these diseases.

### Direct and Indirect Utility of Identified Nucleic Acid Sequences and Related Molecules

The mouse or human genes may be used directly. For diagnostic or screening purposes, they (or specific binding fragments thereof) may be labeled and used as hybridization probes. For therapeutic purposes, they (or specific binding fragments thereof) may be used as antisense reagents to inhibit the expression of the corresponding gene, or of a sufficiently homologous gene of another species.

If the database DNA appears to be a full-length cDNA or gDNA, that is, that it encodes an entire, functional, naturally occurring protein, then it may be used in the expression of that protein. Likewise, if the corresponding human gene is known in full-length, it may be used to express the human protein. Such expression may be in cell culture, with the protein subsequently isolated and administered exogenously to subjects who would benefit therefrom, or in vivo, i.e., administration by gene therapy. Naturally, any DNA encoding the same protein may be used for the same purpose, or a DNA which encodes a fragment or a mutant of that naturally occurring protein which retains the desired activity may be used for the purpose of producing the active fragment or mutant. The encoded protein of course has utility therapeutically and, in labeled or immobilized form, diagnostically.

The genes may also be used indirectly, that is, to

identify other useful DNAs, proteins, or other molecules. We have attempted to determine whether the mouse genes disclosed herein have significant similarity to any known human DNA, and whether, in any of the six possible combinations of reference frame and strand, they encode a protein similar to a known human protein. If so, then it follows that the known human protein, and DNAs encoding that protein, may be used in a similar manner. In addition, if the known human protein is known to have additional homologues, then those homologous proteins, and DNAs encoding them, may be used in a similar manner.

There thus are several ways that a human protein homologue of interest can be identified by database searching, including:

- 1) a DNA->DNA (BlastN) search for human database DNAs closely related to the mouse gene identifies a known human gene, and the sequence of the human protein is deduced by the Genetic Code;
- 2) a DNA->Protein (BlastX) search for human database proteins closely related to the translated DNA of the mouse gene identifies a known human protein; and
- 3) the sequence of the mouse protein is known or is deduced by the Genetic Code, and a Protein->Protein (BlastP) search for closely related database proteins identifies a known human protein.

Once a known human gene is identified, it may be used in further BlastN or BlastX searches to identify other human genes or proteins. Once a known human protein is identified, it may be used in further BlastP searches to identify other human proteins. Searches may also take cognizance, intermediately, of known genes and proteins



other than mouse or human ones, e.g., use the mouse sequence to identify a known rat sequence and then the rat sequence to identify a human one.

5           If we have identified a mouse gene (gDNA or cDNA), and it encodes a mouse protein which appears similar to a human protein, then that human protein may be used (especially in humans) for purposes analogous to the proposed use of the mouse protein in mice. Moreover, a specific binding  
10       fragment of an appropriate strand of the corresponding human gene (gDNA or cDNA) could be labeled and used as a hybridization probe (especially against samples of human mRNA or cDNA).

15           In determining whether the disclosed genes (gDNA or cDNA) have significant similarities to known DNAs (and their translated AA sequences to known proteins), one would generally use the disclosed gene as a query sequence in a search of a sequence database. The results of several such searches are set forth in the Examples. Such results are  
20       dependent, to some degree, on the search parameters. Preferred parameters are set forth in Example 1. The results are also dependent on the content of the database. While the raw similarity score of a particular target (database) sequence will not vary with content (as long as it remains in the database), its informational value (in  
25       bits), expected value, and relative ranking can change. Generally speaking, the changes are small.

30           It will be appreciated that the nucleic acid and protein databases keep growing. Hence a later search may identify high scoring target sequences which were not uncovered by an earlier search because the target sequences were not previously part of a database.

35           Hence, in a preferred embodiment, the cognate DNAs and proteins include not only those set forth in the examples,

but those which would have been highly ranked (top ten, more preferably top three, even more preferably top two, most preferably the top one) in a search run with the same parameters on the date of filing of this application.

If the mouse or human database DNA appears to be a partial DNA (that is, partial relative to a cDNA or gDNA encoding the whole naturally occurring protein), it may be used as a hybridization probe to isolate the full-length DNA. If the partial DNA encodes a biologically functional fragment of the cognate protein, it may be used in a manner similar to the full length DNA, i.e., to produce the functional fragment.

If we have indicated that an antagonist of a protein or other molecule is useful, then such an antagonist may be obtained by preparing a combinatorial library, as described below, of potential antagonists, and screening the library members for binding to the protein or other molecule in question. The binding members may then be further screened for the ability to antagonize the biological activity of the target. The antagonists may be used therapeutically, or, in suitably labeled or immobilized form, diagnostically.

If the mouse or human database DNA is related to a known protein, then substances known to interact with that protein (e.g., agonists, antagonists, substrates, receptors, second messengers, regulators, and so forth), and binding molecules which bind them, are also of utility. Such binding molecules can likewise be identified by screening a combinatorial library.

#### Isolation of Full Length DNAs Using Partial DNAs as probes

If it is determined that a DNA of the present invention is a partial DNA, and the cognate full length DNA is not listed in a sequence database, the available DNA may be used as a hybridization probe to isolate the full-length DNA from

61

a suitable DNA library (cDNA or gDNA).

Stringent hybridization conditions are appropriate, that is, conditions in which the hybridization temperature is 5-10 deg. C. below the  $T_m$  of the DNA as a perfect duplex.

#### Identification and Isolation of Homologous Genes Using a DNA Probe

It may be that the sequence databases available do not include the sequence of any homologous gene (gDNA or cDNA), or at least of the homologous gene for a species of interest. However, given the DNAs set forth above, one may readily obtain the homologous gene.

The possession of one DNA (the "starting DNA") greatly facilitates the isolation of homologous DNAs. If only a partial DNA is known, this partial DNA may first be used as a probe to isolate the corresponding full length DNA for the same species, and that the latter may be used as the starting DNA in the search for homologous DNAs.

The starting DNA, or a fragment thereof, is used as a hybridization probe to screen a cDNA or genomic DNA library for clones containing inserts which encode either the entire homologous protein, or a recognizable fragment thereof. The minimum length of the hybridization probe is dictated by the need for specificity. If the size of the library in bases is  $L$ , and the GC content is 50%, then the probe should have a length of at least  $l$ , where  $L = 4^l$ . This will yield, on average, a single perfect match in random DNA of  $L$  bases. The human cDNA library is about  $10^8$  bases and the human genomic DNA library is about  $10^{10}$  bases.

The library is preferably derived from an organism which is known, on biochemical evidence, to produce a homologous protein, and more preferably from the genomic DNA or mRNA of cells of that organism which are likely to be relatively high producers of that protein. A cDNA library (which is derived from an mRNA library) is especially preferred.

If the organism in question is known to have substantially different codon preferences from that of the organism whose relevant cDNA or genomic DNA is known, a synthetic hybridization probe may be used which encodes the same amino acid sequence but whose codon utilization is more similar to that of the DNA of the target organism. Alternatively, the synthetic probe may employ inosine as a substitute for those bases which are most likely to be divergent, or the probe may be a mixed probe which mixes the codons for the source DNA with the preferred codons (encoding the same amino acid) for the target organism.

By routine methods, the  $T_m$  of a perfect duplex of starting DNA is determined. One may then select a hybridization temperature which is sufficiently lower than the perfect duplex  $T_m$  to allow hybridization of the starting DNA (or other probe) to a target DNA which is divergent from the starting DNA. A 1% sequence divergence typically lowers the  $T_m$  of a duplex by 1-2°C, and the DNAs encoding homologous proteins of different species typically have sequence identities of around 50-80%. Preferably, the library is screened under conditions where the temperature is at least 20°C., more preferably at least 50°C., below the perfect duplex  $T_m$ . Since salt reduces the  $T_m$ , one ordinarily would carry out the search for DNAs encoding highly homologous proteins under relatively low salt hybridization conditions, e.g., <1M NaCl. The higher the salt concentration, and/or the lower the temperature, the greater the sequence divergence which is tolerated.

For the use of probes to identify homologous genes in other species, see, e.g., Schwinn, et al., J. Biol. Chem., 265:8183-89 (1990) (hamster 67-bp cDNA probe vs. human leukocyte genomic library; human 0.32kb DNA probe vs. bovine brain cDNA library, both with hybridization at 42°C in 6xSSC); Jenkins et al., J. Biol. Chem., 265:19624-31 (1990) (Chicken 770-bp cDNA probe vs. human genomic libraries; hybridization at 40°C in 50% formamide and 5xSSC); Murata et

al., J. Exp. Med., 175:341-51 (1992) (1.2-kb mouse cDNA probe v. human eosinophil cDNA library; hybridization at 65°C in 6xSSC); Guyer et al., J. Biol. Chem., 265:17307-17 (1990) (2.95-kb human genomic DNA probe vs. porcine genomic DNA library; hybridization at 42°C in 5xSSC). The conditions set forth in these articles may each be considered suitable for the purpose of isolating homologous genes.

#### Corresponding (Homologous) Proteins and DNAs

In the case of a gene chip, the manufacturer of the gene chip determines which DNA to place at each position on the chip. This DNA may correspond in sequence to a genomic DNA, a cDNA, or a fragment of genomic or cDNA, and may be natural, synthetic or partially natural and partially synthetic in origin. The manufacturer of the gene chip will normally identify the DNA for a mouse gene chip as corresponding to a particular mouse gene, in which case it will be assumed that the alignments of chip DNA to mouse gene satisfies the correspondence (homology) criteria of the invention.

Usually, the gene chip manufacturer will provide a sequence database accession number for the mouse DNA. If so, to identify the corresponding mouse protein, we will first inspect the database record for that mouse DNA. Often, the mouse protein accession number will appear in that record or in a linked record. If it doesn't, the corresponding mouse protein can be identified by performing a BlastX search on a mouse protein database with the mouse database DNA sequence as the query sequence. Even if the protein sequence is not in the database, if the DNA sequence comprises a full-length coding sequence, the corresponding protein can be identified by translating the coding sequence in accordance with the Genetic Code.

A human protein can be said to be identifiable as

corresponding (homologous) to a gene chip DNA if it is identified as corresponding (homologous) to the mouse gene (gDNA or cDNA, whole or partial) identified by the gene chip manufacturer as corresponding (homologous) to that gene chip DNA.

In turn, it is identifiable as corresponding (homologous) to said identified mouse gene, if

(1) it can be aligned by BlastX directly to that mouse gene, and/or

(2) it is encoded by a human gene, or can be aligned to a human gene by BlastX, which in turn can be aligned by BlastN to said mouse gene and/or

(3) it can be aligned by BlastP to a mouse protein, the latter being encoded by said mouse gene, or aligned to said mouse gene BlastX,

where any alignment by BlastN, BlastP or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone) is less than  $e^{-10}$ . (Note that because this is a negative exponent, a value such as  $e^{-50}$  is less than  $e^{-10}$ .)

A human gene is corresponding (homologous) to a mouse gene chip DNA, and hence to said identified mouse gene (or cDNA) and protein, if it encodes a corresponding (homologous) human protein as defined above, or it can be aligned by BlastN to said mouse gene.

Desirably, two or all three of these conditions (1)-(3) are satisfied for the corresponding (homologous) human genes and proteins.

Preferably, for at least one of conditions (1)-(3), the E value is less than e-50, more preferably less than e-60, still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100. Desirably, it is true for two or even all three of these conditions.

In constructing Master table 1, we generally used a BlastX (mouse gene vs. human protein) alignment E value cutoff of e-50. However, if there were no human proteins with that good an alignment to the mouse DNA in question, or if there were other reasons for including a particular human protein (e.g., a known functionality supportive of the observed differential cognate mouse protein expression), then a human protein with a score worse (i.e., higher) than e-50 may appear in Master Table 1.

BlastN and BlastX report very low expected values as "0.0". This does not truly mean that the expected value is exactly zero (since any alignment could occur by chance), but merely that it is so infinitesimal that it is not reported. The documentation does not state the cutoff value, alignments with explicit E values as low as e-178 (624 bits) have been reported as such, while a score of 636 bits was reported as "0.0".

If the manufacturer of the gene chip identifies the gene chip DNA as corresponding to an EST, or other DNA which is not a full-length mouse gene or cDNA, a longer (possibly full length) mouse gene or cDNA may be identified by a BlastN search of the mouse DNA database. Alternatively, the identified DNA may be used to conduct a BlastN search of a human DNA database, or a BlastX search of a mouse or human protein database.

Thus, more generally, a human protein can be said to be

identifiable as corresponding (homologous) to a gene chip DNA, or to a DNA identified by the manufacturer as corresponding to that gene chip DNA, if

(1') it can be aligned directly to the gene chip or corresponding manufacturer identified DNA by BlastX. and/or

(2') it can be aligned to a human gene/cDNA by BlastX, whose genomic DNA (gDNA) or cDNA (DNA complementary to messenger RNA) in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or

(3') it can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or

(4') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastX, and/or

(5') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA can in turn be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN;

where any alignment by BlastN, BlastP, or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone) is less than  $e^{-10}$ . (Note that because this is a negative exponent, a value such as  $e^{-50}$  is less than  $e^{-10}$ .)

Preferably, two, three, four or all five of conditions (1')-(5') are satisfied.

Preferably, for at least one of conditions (1')-(5'), for at least the final alignment (i.e., vs. the human



67

protein), the E value is less than e-50, more preferably less than e-60, , still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100.

5 Desirably, one or more of these standards of preference are met for two, three, four or all five of conditions (1')-(5'). In particular, for those conditions in which the gene chip or corresponding manufacturer identified DNA is indirectly connected to the human protein by virtue of two  
10 or more successive alignments, the E value is preferably, so limited for all of said alignments in the connecting chain.

A human gene corresponds (is homologous) to a gene chip DNA or manufacturer identified corresponding DNA if it encodes a corresponding (homologous) human protein as  
15 defined above, or if it can be aligned either directly to that DNA, or indirectly through a mouse gene which can be aligned to said DNA, according to the conditions set forth above.

20 Master table 1 assembles a list of human protein corresponding (homologous) to each of the mouse DNAs/proteins identified as related to the chip DNA. These human proteins form a set and can be given a percentile rank, with respect to E value, within that set. The human  
25 proteins of the present invention preferably are those scorers with a percentile rank of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

0 For each mouse gene in Master Table 1, there is a particular human protein which provides the best alignment match as measured by BlastX, i.e., the human protein with the best score (lowest e-value). These human proteins form  
5 a subset of the set above and can be given a percentile rank within that subset, e.g., the human proteins with scores in

the top 10% of that subset have a percentile rank of 90% or higher.

The human proteins of the present invention preferably are those best scorer subset proteins with a percentile rank within the subset of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

BlastN and BlastX report very low expected values as "0.0". This does not truly mean that the expected value is exactly zero (since any alignment could occur by chance), but merely that it is so infinitesimal that it is not reported. The documentation does not state the cutoff value, but alignments with explicit E values as low as  $e^{-178}$  (624 bits) have been reported as nonzero values, while a score of 636 bits was reported as "0.0".

Functionally homologous human proteins are also of interest. A human protein may be said to be functionally homologous to the mouse gene if the human protein has at least one biological activity in common with the mouse protein encoded by said mouse gene.

The human proteins of interest also include those that are substantially and/or conservatively identical (as defined below) to the homologous and/or functionally homologous human proteins defined above.

#### Degree of Differential Expression

The degree of differential expression may be expressed as the ratio of the higher expression level to the lower expression level. Preferably, this is at least 2-fold, and more preferably, it is higher, such as at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold.

Most preferably, the human protein of interest

corresponds to a mouse gene for which the degree of differential expression places it among the top 10% of the mouse genes in the appropriate subtable.

#### 5 Relevance of Favorable and Unfavorable Genes

If a gene is down-regulated in more favored mammals, or up-regulated in less favored mammals, (i.e., an "unfavorable gene") then several utilities are apparent.

10 First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Elevated levels are indicative of progression, or propensity to progression, to a less favored state, and  
15 clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product (or equivalent cDNA), the protein product, or a binding molecule specific for that product (e.g., an antibody which binds the  
20 product), or a downstream product which mediates the activity (e.g., a signaling intermediate) or a binding molecule (e.g., an antibody) therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said nucleic acid product, protein  
25 product, or downstream product (e.g., a signaling intermediate). Again, elevated levels are indicative of a present or future problem.

Thirdly, an agent which down-regulates expression of the gene may be used to reduce levels of the corresponding  
30 protein and thereby inhibit further damage. This agent could inhibit transcription of the gene in the subject, or translation of the corresponding messenger RNA. Possible inhibitors of transcription and translation include antisense molecules and repressor molecules. The agent  
35 could also inhibit a post-translational modification (e.g., glycosylation, phosphorylation, cleavage, GPI attachment)

required for activity, or post-translationally modify the protein so as to inactivate it. Or it could be an agent which down- or up-regulated a positive or negative regulatory gene, respectively.

Fourthly, an agent which is an antagonist of the messenger RNA product or protein product of the gene, or of a downstream product through which its activity is manifested (e.g., a signaling intermediate), may be used to inhibit its activity.

This antagonist could be an antibody, a peptide, a peptoid, a nucleic acid, a peptide nucleic acid (PNA) oligomer, a small organic molecule of a kind for which a combinatorial library exists (e.g., a benzodiazepine), etc. An antagonist is simply a binding molecule which, by binding, reduces or abolishes the undesired activity of its target. The antagonist, if not an oligomeric molecule, is preferably less than 1000 daltons, more preferably less than 500 daltons.

Fifthly, an agent which degrades, or abets the degradation of, that messenger RNA, its protein product or a downstream product which mediates its activity (e.g., a signaling intermediate), may be used to curb the effective period of activity of the protein.

If a gene is up-regulated in more favored mammals, or down-regulated in less favored animals then the utilities are converse to those stated above.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Depressed levels are indicative of damage, or possibly of a propensity to damage, and clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product, the equivalent cDNA, protein product, or a binding molecule specific for those products, or a downstream product, or a signaling

intermediate, or a binding molecule therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said protein product or downstream product. Again, depressed levels are indicative of a present or future problem.

Thirdly, an agent which up-regulates expression of the gene may be used to increase levels of the corresponding protein and thereby inhibit further progression to a less favored state. By way of example, it could be a vector which carries a copy of the gene, but which expresses the gene at higher levels than does the endogenous expression system. Or it could be an agent which up- or down-regulates a positive or negative regulatory gene.

Fourthly, an agent which is an agonist of the protein product of the gene, or of a downstream product through which its activity (of inhibition of progression to a less favored state) is manifested, or of a signaling intermediate may be used to foster its activity.

Fifthly, an agent which inhibits the degradation of that protein product or of a downstream product or of a signaling intermediate may be used to increase the effective period of activity of the protein.

#### **Mutant Proteins**

The present invention also contemplates mutant proteins (peptides) which are substantially identical (as defined below) to the parental protein (peptide). In general, the fewer the mutations, the more likely the mutant protein is to retain the activity of the parental protein. The effect of mutations is usually (but not always) additive. Certain individual mutations are more likely to be tolerated than others.

A protein is more likely to tolerate a mutation which

(a) is a substitution rather than an insertion or deletion;

72

(b) is an insertion or deletion at the terminus, rather than internally, or, if internal, is at a domain boundary, or a loop or turn, rather than in an alpha helix or beta strand;

(c) affects a surface residue rather than an interior residue;

(d) affects a part of the molecule distal to the binding site;

(e) is a substitution of one amino acid for another of similar size, charge, and/or hydrophobicity, and does not destroy a disulfide bond or other crosslink; and

(f) is at a site which is subject to substantial variation among a family of homologous proteins to which the protein of interest belongs.

These considerations can be used to design functional mutants.

#### *Surface vs. Interior Residues*

Charged amino acid residues almost always lie on the surface of the protein. For uncharged residues, there is less certainty, but in general, hydrophilic residues are partitioned to the surface and hydrophobic residues to the interior. Of course, for a membrane protein, the membrane-spanning segments are likely to be rich in hydrophobic residues.

Surface residues may be identified experimentally by various labeling techniques, or by 3-D structure mapping techniques like X-ray diffraction and NMR. A 3-D model of a homologous protein can be helpful.

#### *Binding Site Residues*

Residues forming the binding site may be identified by (1) comparing the effects of labeling the surface residues before and after complexing the protein to its target, (2) labeling the binding site directly with affinity ligands,

(3) fragmenting the protein and testing the fragments for binding activity, and (4) systematic mutagenesis (e.g., alanine-scanning mutagenesis) to determine which mutants destroy binding. If the binding site of a homologous protein is known, the binding site may be postulated by analogy.

Protein libraries may be constructed and screened that a large family (e.g.,  $10^8$ ) of related mutants may be evaluated simultaneously.

Hence, the mutations are preferably conservative modifications as defined below.

#### "Substantially Identical"

A mutant protein (peptide) is substantially identical to a reference protein (peptide) if (a) it has at least 10% of a specific binding activity or a non-nutritional biological activity of the reference protein, and (b) is at least 50% identical in amino acid sequence to the reference protein (peptide). It is "substantially structurally identical" if condition (b) applies, regardless of (a).

Percentage amino acid identity is determined by aligning the mutant and reference sequences according to a rigorous dynamic programming algorithm which globally aligns their sequences to maximize their similarity, the similarity being scored as the sum of scores for each aligned pair according to an unbiased PAM250 matrix, and a penalty for each internal gap of -12 for the first null of the gap and -4 for each additional null of the same gap. The percentage identity is the number of matches expressed as a percentage of the adjusted (i.e., counting inserted nulls) length of the reference sequence.

A mutant DNA sequence is substantially identical to a reference DNA sequence if they are structural sequences, and encoding mutant and reference proteins which are substantially identical as described above.

If instead they are regulatory sequences, they are

substantially identical if the mutant sequence has at least 10% of the regulatory activity of the reference sequence, and is at least 50% identical in nucleotide sequence to the reference sequence. Percentage identity is determined as for proteins except that matches are scored +5, mismatches -4, the gap open penalty is -12, and the gap extension penalty (per additional null) is -4.

More preferably, the sequence is not merely substantially identical, but rather is at least 51%, 66%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical in sequence to the reference sequence.

DNA sequences may also be considered "substantially identical" if they hybridize to each other under stringent conditions, i.e., conditions at which the  $T_m$  of the heteroduplex of the one strand of the mutant DNA and the more complementary strand of the reference DNA is not in excess of 10°C. less than the  $T_m$  of the reference DNA homoduplex. Typically this will correspond to a percentage identity of 85-90%.

#### "Conservative Modifications"

"Conservative modifications" are defined as

(a) conservative substitutions of amino acids as hereafter defined; or

(b) single or multiple insertions (extension) or deletions (truncation) of amino acids at the termini.

Conservative modifications are preferred to other modifications. Conservative substitutions are preferred to other conservative modifications.

"Semi-Conservative Modifications" are modifications which are not conservative, but which are (a) semi-conservative substitutions as hereafter defined; or (b) single or multiple insertions or deletions internally, but at interdomain boundaries, in loops or in other segments of relatively high mobility. Semi-conservative modifications



are preferred to nonconservative modifications. Semi-conservative substitutions are preferred to other semi-conservative modifications.

Non-conservative substitutions are preferred to other non-conservative modifications.

The term "conservative" is used here in an a priori sense, i.e., modifications which would be expected to preserve 3D structure and activity, based on analysis of the naturally occurring families of homologous proteins and of past experience with the effects of deliberate mutagenesis, rather than post facto, a modification already known to conserve activity. Of course, a modification which is conservative a priori may, and usually is, also conservative post facto.

Preferably, except at the termini, no more than about five amino acids are inserted or deleted at a particular locus, and the modifications are outside regions known to contain binding sites important to activity.

Preferably, insertions or deletions are limited to the termini.

A conservative substitution is a substitution of one amino acid for another of the same exchange group, the exchange groups being defined as follows

- I Gly, Pro, Ser, Ala (Cys) (and any nonbiogenic, neutral amino acid with a hydrophobicity not exceeding that of the aforementioned a.a.'s)
- II Arg, Lys, His (and any nonbiogenic, positively-charged amino acids)
- III Asp, Glu, Asn, Gln (and any nonbiogenic negatively-charged amino acids)
- IV Leu, Ile, Met, Val (Cys) (and any nonbiogenic, aliphatic, neutral amino acid with a hydrophobicity too high for I above)
- V Phe, Trp, Tyr (and any nonbiogenic, aromatic neutral amino acid with a hydrophobicity too high for I above).

Note that Cys belongs to both I and IV.

Residues Pro; Gly and Cys have special conformational roles. Cys participates in formation of disulfide bonds. Gly imparts flexibility to the chain. Pro imparts rigidity to the chain and disrupts  $\alpha$  helices. These residues may be essential in certain regions of the polypeptide, but substitutable elsewhere.

One, two or three conservative substitutions are more likely to be tolerated than a larger number.

"Semi-conservative substitutions" are defined herein as being substitutions within supergroup I/II/III or within supergroup IV/V, but not within a single one of groups I-V. They also include replacement of any other amino acid with alanine. If a substitution is not conservative, it preferably is semi-conservative.

"Non-conservative substitutions" are substitutions which are not "conservative" or "semi-conservative".

"Highly conservative substitutions" are a subset of conservative substitutions, and are exchanges of amino acids within the groups Phe/Tyr/Trp, Met/Leu/Ile/Val, His/Arg/Lys, Asp/Glu and Ser/Thr/Ala. They are more likely to be tolerated than other conservative substitutions. Again, the smaller the number of substitutions, the more likely they are to be tolerated.

#### "Conservatively Identical"

A protein (peptide) is conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by conservative modifications, the protein (peptide) remaining at least seven amino acids long if the reference protein (peptide) was at least seven amino acids long.

A protein is at least semi-conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by semi-conservative or conservative modifications.

A protein (peptide) is nearly conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by one or more conservative modifications and/or a single nonconservative substitution.

It is highly conservatively identical if it differs, if at all, solely by highly conservative substitutions. Highly conservatively identical proteins are preferred to those merely conservatively identical. An absolutely identical protein is even more preferred.

The core sequence of a reference protein (peptide) is the largest single fragment which retains at least 10% of a particular specific binding activity, if one is specified, or otherwise of at least one specific binding activity of the referent. If the referent has more than one specific binding activity, it may have more than one core sequence, and these may overlap or not.

If it is taught that a peptide of the present invention may have a particular similarity relationship (e.g., markedly identical) to a reference protein (peptide), preferred peptides are those which comprise a sequence having that relationship to a core sequence of the reference protein (peptide), but with internal insertions or deletions in either sequence excluded. Even more preferred peptides are those whose entire sequence has that relationship, with the same exclusion, to a core sequence of that reference protein (peptide).

#### Library

The term "library" generally refers to a collection of chemical or biological entities which are related in origin, structure, and/or function, and which can be screened simultaneously for a property of interest.

Libraries may be classified by how they are constructed

(natural vs. artificial diversity; combinatorial vs. noncombinatorial), how they are screened (hybridization, expression, display), or by the nature of the screened library members (peptides, nucleic acids, etc.).

In a "natural diversity" library, essentially all of the diversity arose without human intervention. This would be true, for example, of messenger RNA extracted from a non-engineered cell.

In a "synthetic diversity" library, essentially all of the diversity arose deliberately as a result of human intervention. This would be true for example of a combinatorial library; note that a small level of natural diversity could still arise as a result of spontaneous mutation. It would also be true of a noncombinatorial library of compounds collected from diverse sources, even if they were all natural products.

In a "non-natural diversity" library, at least some of the diversity arose deliberately through human intervention.

In a "controlled origin" library, the source of the diversity is limited in some way. A limitation might be to cells of a particular individual, to a particular species, or to a particular genus, or, more complexly, to individuals of a particular species who are of a particular age, sex, physical condition, geographical location, occupation and/or familial relationship. Alternatively or additionally, it might be to cells of a particular tissue or organ. Or it could be cells exposed to particular pharmacological, environmental, or pathogenic conditions. Or the library could be of chemicals, or a particular class of chemicals, produced by such cells.

In a "controlled structure" library, the library members are deliberately limited by the production conditions to particular chemical structures. For example, if they are oligomers, they may be limited in length and monomer composition, e.g. hexapeptides composed of the twenty genetically encoded amino acids.

### Hybridization Library

In a hybridization library, the library members are nucleic acids, and are screened using a nucleic acid hybridization probe. Bound nucleic acids may then be amplified, cloned, and/or sequenced.

### Expression Library

In an expression library, the screened library members are gene expression products, but one may also speak of an underlying library of genes encoding those products. The library is made by subcloning DNA encoding the library members (or portions thereof) into expression vectors (or into cloning vectors which subsequently are used to construct expression vectors), each vector comprising an expressible gene encoding a particular library member, introducing the expression vectors into suitable cells, and expressing the genes so the expression products are produced.

In one embodiment, the expression products are secreted, so the library can be screened using an affinity reagent, such as an antibody or receptor. The bound expression products may be sequenced directly, or their sequences inferred by, e.g., sequencing at least the variable portion of the encoding DNA.

In a second embodiment, the cells are lysed, thereby exposing the expression products, and the latter are screened with the affinity reagent.

In a third embodiment, the cells express the library members in such a manner that they are displayed on the surface of the cells, or on the surface of viral particles produced by the cells. (See display libraries, below).

In a fourth embodiment, the screening is not for the ability of the expression product to bind to an affinity reagent, but rather for its ability to alter the phenotype of the host cell in a particular detectable manner. Here, the screened library members are transformed cells, but

there is a first underlying library of expression products which mediate the behavior of the cells, and a second underlying library of genes which encode those products.

#### Display Library

In a display library, the library members are each conjugated to, and displayed upon, a support of some kind. The support may be living (a cell or virus), or nonliving (e.g., a bead or plate).

If the support is a cell or virus, display will normally be effectuated by expressing a fusion protein which comprises the library member, a carrier moiety allowing integration of the fusion protein into the surface of the cell or virus, and optionally a lining moiety. In a variation on this theme, the cell coexpresses a first fusion comprising the library member and a linking moiety L1, and a second fusion comprising a linking moiety L2 and the carrier moiety. L1 and L2 interact to associate the first fusion with the second fusion and hence, indirectly, the library member with the surface of the cell or virus.

#### Soluble Library

In a soluble library, the library members are free in solution. A soluble library may be produced directly, or one may first make a display library and then release the library members from their supports.

#### Encapsulated Library

In an encapsulated library, the library members are inside cells or liposomes. Generally speaking, encapsulated libraries are used to store the library members for future use; the members are extracted in some way for screening purposes. However, if they differentially affect the phenotype of the cells, they may be screened indirectly by screening the cells.

cDNA Library

A cDNA library is usually prepared by extracting RNA from cells of particular origin, fractionating the RNA to isolate the messenger RNA (mRNA has a poly(A) tail, so this is usually done by oligo-dT affinity chromatography), synthesizing complementary DNA (cDNA) using reverse transcriptase, DNA polymerase, and other enzymes, subcloning the cDNA into vectors, and introducing the vectors into cells. Often, only mRNAs or cDNAs of particular sizes will be used, to make it more likely that the cDNA encodes a functional polypeptide.

A cDNA library explores the natural diversity of the transcribed DNAs of cells from a particular source. It is not a combinatorial library.

A cDNA library may be used to make a hybridization library, or it may be used as an (or to make) expression library.

Genomic DNA Library

A genomic DNA library is made by extracting DNA from a particular source, fragmenting the DNA, isolating fragments of a particular size range, subcloning the DNA fragments into vectors, and introducing the vectors into cells.

Like a cDNA library, a genomic DNA library is a natural diversity library, and not a combinatorial library. A genomic DNA library may be used the same way as a cDNA library.

Synthetic DNA library

A synthetic DNA library may be screened directly (as a hybridization library), or used in the creation of an expression or display library of peptides/proteins.

Combinatorial Libraries

The term "combinatorial library" refers to a library in which the individual members are either systematic or random

combinations of a limited set of basic elements, the properties of each member being dependent on the choice and location of the elements incorporated into it. Typically, the members of the library are at least capable of being screened simultaneously. Randomization may be complete or partial; some positions may be randomized and others predetermined, and at random positions, the choices may be limited in a predetermined manner. The members of a combinatorial library may be oligomers or polymers of some kind, in which the variation occurs through the choice of monomeric building block at one or more positions of the oligomer or polymer, and possibly in terms of the connecting linkage, or the length of the oligomer or polymer, too. Or the members may be nonoligomeric molecules with a standard core structure, like the 1,4-benzodiazepine structure, with the variation being introduced by the choice of substituents at particular variable sites on the core structure. Or the members may be nonoligomeric molecules assembled like a jigsaw puzzle, but wherein each piece has both one or more variable moieties (contributing to library diversity) and one or more constant moieties (providing the functionalities for coupling the piece in question to other pieces).

Thus, in a typical combinatorial library, chemical building blocks are at least partially randomly combined into a large number (as high as  $10^{15}$ ) of different compounds, which are then simultaneously screened for binding (or other) activity against one or more targets.

In a "simple combinatorial library", all of the members belong to the same class of compounds (e.g., peptides) and can be synthesized simultaneously. A "composite combinatorial library" is a mixture of two or more simple libraries, e.g., DNAs and peptides, or peptides, peptoids, and PNAs, or benzodiazepines and carbamates. The number of component simple libraries in a composite library will, of course, normally be smaller than the average number of members in each simple library, as otherwise the advantage



of a library over individual synthesis is small.

Libraries of thousands, even millions, of random oligopeptides have been prepared by chemical synthesis (Houghten et al., Nature, 354:84-6(1991)), or gene expression (Marks et al., J Mol Biol, 222:581-97(1991)), displayed on chromatographic supports (Lam et al., Nature, 354:82-4(1991)), inside bacterial cells (Colas et al., Nature, 380:548-550(1996)), on bacterial pili (Lu, Bio/Technology, 13:366-372(1990)), or phage (Smith, Science, 228:1315-7(1985)), and screened for binding to a variety of targets including antibodies (Valadon et al., J Mol Biol, 261:11-22(1996)), cellular proteins (Schmitz et al., J Mol Biol, 260:664-677(1996)), viral proteins (Hong and Boulanger, Embo J, 14:4714-4727(1995)), bacterial proteins (Jacobsson and Frykberg, Biotechniques, 18:878-885(1995)), nucleic acids (Cheng et al., Gene, 171:1-8(1996)), and plastic (Siani et al., J Chem Inf Comput Sci, 34:588-593(1994)).

Libraries of proteins (Ladner, USP 4,664,989), peptoids (Simon et al., Proc Natl Acad Sci U S A, 89:9367-71(1992)), nucleic acids (Ellington and Szostak, Nature, 246:818(1990)), carbohydrates, and small organic molecules (Eichler et al., Med Res Rev, 15:481-96(1995)) have also been prepared or suggested for drug screening purposes.

The first combinatorial libraries were composed of peptides or proteins, in which all or selected amino acid positions were randomized. Peptides and proteins can exhibit high and specific binding activity, and can act as catalysts. In consequence, they are of great importance in biological systems.

Nucleic acids have also been used in combinatorial libraries. Their great advantage is the ease with which a nucleic acid with appropriate binding activity can be amplified. As a result, combinatorial libraries composed of nucleic acids can be of low redundancy and hence, of high diversity.

There has also been much interest in combinatorial libraries based on small molecules, which are more suited to pharmaceutical use, especially those which, like benzodiazepines, belong to a chemical class which has already yielded useful pharmacological agents. The techniques of combinatorial chemistry have been recognized as the most efficient means for finding small molecules that act on these targets. At present, small molecule combinatorial chemistry involves the synthesis of either pooled or discrete molecules that present varying arrays of functionality on a common scaffold. These compounds are grouped in libraries that are then screened against the target of interest either for binding or for inhibition of biological activity.

The size of a library is the number of molecules in it. The simple diversity of a library is the number of unique structures in it. There is no formal minimum or maximum diversity. If the library has a very low diversity, the library has little advantage over just synthesizing and screening the members individually. If the library is of very high diversity, it may be inconvenient to handle, at least without automatizing the process. The simple diversity of a library is preferably at least  $10^1$ ,  $10^2$ ,  $10^3$ ,  $10^4$ ,  $10^6$ ,  $10^7$ ,  $10^8$  or  $10^9$ , the higher the better under most circumstances. The simple diversity is usually not more than  $10^{15}$ , and more usually not more than  $10^{10}$ .

The average sampling level is the size divided by the simple diversity. The expected average sampling level must be high enough to provide a reasonable assurance that, if a given structure were expected, as a consequence of the library design, to be present, that the actual average sampling level will be high enough so that the structure, if satisfying the screening criteria, will yield a positive result when the library is screened. Thus, the preferred average sampling level is a function of the detection limit, which in turn is a function of the strength of the signal to

be screened.

There are more complex measures of diversity than simple diversity. These attempt to take into account the degree of structural difference between the various unique sequences. These more complex measures are usually used in the context of small organic compound libraries, see below.

The library members may be presented as solutes in solution, or immobilized on some form of support. In the latter case, the support may be living (cell, virus) or nonliving (bead, plate, etc.). The supports may be separable (cells, virus particles, beads) so that binding and nonbinding members can be separated, or nonseparable (plate). In the latter case, the members will normally be placed on addressable positions on the support. The advantage of a soluble library is that there is no carrier moiety that could interfere with the binding of the members to the support. The advantage of an immobilized library is that it is easier to identify the structure of the members which were positive.

When screening a soluble library, or one with a separable support, the target is usually immobilized. When screening a library on a nonseparable support, the target will usually be labeled.

#### Oligonucleotide Libraries

An oligonucleotide library is a combinatorial library, at least some of whose members are single-stranded oligonucleotides having three or more nucleotides connected by phosphodiester or analogous bonds. The oligonucleotides may be linear, cyclic or branched, and may include non-nucleic acid moieties. The nucleotides are not limited to the nucleotides normally found in DNA or RNA. For examples of nucleotides modified to increase nuclease resistance and chemical stability of aptamers, see Chart 1 in Osborne and Ellington, Chem. Rev., 97: 349-70 (1997). For screening of RNA, see Ellington and Szostak, Nature, 346: 818-22 (1990).

There is no formal minimum or maximum size for these oligonucleotides: However, the number of conformations which an oligonucleotide can assume increases exponentially with its length in bases. Hence, a longer oligonucleotide is more likely to be able to fold to adapt itself to a protein surface. On the other hand, while very long molecules can be synthesized and screened, unless they provide a much superior affinity to that of shorter molecules, they are not likely to be found in the selected population, for the reasons explained by Osborne and Ellington (1997). Hence, the libraries of the present invention are preferably composed of oligonucleotides having a length of 3 to 100 bases, more preferably 15 to 35 bases. The oligonucleotides in a given library may be of the same or of different lengths.

Oligonucleotide libraries have the advantage that libraries of very high diversity (e.g.,  $10^{15}$ ) are feasible, and binding molecules are readily amplified in vitro by polymerase chain reaction (PCR). Moreover, nucleic acid molecules can have very high specificity and affinity to targets.

In a preferred embodiment, this invention prepares and screens oligonucleotide libraries by the SELEX method, as described in King and Famulok, *Molec. Biol. Repts.*, 20: 97-107 (1994); L. Gold, C. Tuerk. *Methods of producing nucleic acid ligands*, US#5595877; Oliphant et al. *Gene* 44:177 (1986).

The term "aptamer" is conferred on those oligonucleotides which bind the target protein. Such aptamers may be used to characterize the target protein, both directly (through identification of the aptamer and the points of contact between the aptamer and the protein) and indirectly (by use of the aptamer as a ligand to modify the chemical reactivity of the protein).

In a classic oligonucleotide, each nucleotide (monomeric unit) is composed of a phosphate group, a sugar moiety, and

either a purine or a pyrimidine base. In DNA, the sugar is deoxyribose and in RNA it is ribose. The nucleotides are linked by 5'-3' phosphodiester bonds.

The deoxyribose phosphate backbone of DNA can be modified to increase resistance to nuclease and to increase penetration of cell membranes. Derivatives such as mono- or dithiophosphates, methyl phosphonates, boranophosphates, formacetals, carbamates, siloxanes, and dimethylenethio- -sulfoxide- and-sulfo- linked species are known in the art.

### Peptide Library

A peptide is composed of a plurality of amino acid residues joined together by peptidyl (-NHCO-) bonds. A biogenic peptide is a peptide in which the residues are all genetically encoded amino acid residues; it is not necessary that the biogenic peptide actually be produced by gene expression.

Amino acids are the basic building blocks with which peptides and proteins are constructed. Amino acids possess both an amino group (-NH<sub>2</sub>) and a carboxylic acid group (-COOH). Many amino acids, but not all, have the alpha amino acid structure NH<sub>2</sub>-CHR-COOH, where R is hydrogen, or any of a variety of functional groups.

Twenty amino acids are genetically encoded: Alanine, Arginine, Asparagine, Aspartic Acid, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, and Valine. Of these, all save Glycine are optically isomeric, however, only the L-form is found in humans. Nevertheless, the D-forms of these amino acids do have biological significance; D-Phe, for example, is a known analgesic.

Many other amino acids are also known, including: 2-Aminoadipic acid; 3-Aminoadipic acid; beta-Aminopropionic acid; 2-Aminobutyric acid; 4-Aminobutyric acid (Piperidinic

acid); 6-Aminocaproic acid; 2-Aminoheptanoic acid; 2-Aminoisobutyric acid, 3-Aminoisobutyric acid; 2'-Aminopimelic acid; 2,4-Diaminobutyric acid; Desmosine; 2,2'-Diaminopimelic acid; 2,3-Diaminopropionic acid; N-Ethylglycine; N-Ethylasparagine; Hydroxylysine; allo-Hydroxylysine; 3-Hydroxyproline; 4-Hydroxyproline; Isodesmosine; allo-Isoleucine; N-Methylglycine (Sarcosine); N-Methylisoleucine; N-Methylvaline; Norvaline; Norleucine; and Ornithine.

Peptides are constructed by condensation of amino acids and/or smaller peptides. The amino group of one amino acid (or peptide) reacts with the carboxylic acid group of a second amino acid (or peptide) to form a peptide (-NHCO-) bond, releasing one molecule of water. Therefore, when an amino acid is incorporated into a peptide, it should, technically speaking, be referred to as an amino acid residue. The core of that residue is the moiety which excludes the -NH and -CO linking functionalities which connect it to other residues. This moiety consists of one or more main chain atoms (see below) and the attached side chains.

The main chain moiety of each amino acid consists of the -NH and -CO linking functionalities and a core main chain moiety. Usually the latter is a single carbon atom. However, the core main chain moiety may include additional carbon atoms, and may also include nitrogen, oxygen or sulfur atoms, which together form a single chain. In a preferred embodiment, the core main chain atoms consist solely of carbon atoms.

The side chains are attached to the core main chain atoms. For alpha amino acids, in which the side chain is attached to the alpha carbon, the C-1, C-2 and N-2 of each residue form the repeating unit of the main chain, and the word "side chain" refers to the C-3 and higher numbered carbon atoms and their substituents. It also includes H atoms attached to the main chain atoms.

Amino acids may be classified according to the number of carbon atoms which appear in the main chain between the carbonyl carbon and amino nitrogen atoms which participate in the peptide bonds. Among the 150 or so amino acids which occur in nature, alpha, beta, gamma and delta amino acids are known. These have 1-4 intermediary carbons. Only alpha amino acids occur in proteins. Proline is a special case of an alpha amino acid; its side chain also binds to the peptide bond nitrogen.

For beta and higher order amino acids, there is a choice as to which main chain core carbon a side chain other than H is attached to. The preferred attachment site is the C-2 (alpha) carbon, i.e., the one adjacent to the carboxyl carbon of the -CO linking functionality. It is also possible for more than one main chain atom to carry a side chain other than H. However, in a preferred embodiment, only one main chain core atom carries a side chain other than H.

A main chain carbon atom may carry either one or two side chains; one is more common. A side chain may be attached to a main chain carbon atom by a single or a double bond; the former is more common.

A simple combinatorial peptide library is one whose members are peptides having three or more amino acids connected via peptide bonds.

The peptides may be linear, branched, or cyclic, and may covalently or noncovalently include nonpeptidyl moieties. The amino acids are not limited to the naturally occurring or to the genetically encoded amino acids.

A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues.

#### *Cyclic Peptides*

Many naturally occurring peptides are cyclic. Cyclization is a common mechanism for stabilization of peptide conformation thereby achieving improved association

of the peptide with its ligand and hence improved biological activity. Cyclization is usually achieved by intra-chain cystine formation, by formation of peptide bond between side chains or between N- and C- terminals. Cyclization was usually achieved by peptides in solution, but several publications have appeared that describe cyclization of peptides on beads.

A peptide library may be an oligopeptide library or a protein library.

### *Oligopeptides*

Preferably, the oligopeptides are at least five, six, seven or eight amino acids in length. Preferably, they are composed of less than 50, more preferably less than 20 amino acids.

In the case of an oligopeptide library, all or just some of the residues may be variable. The oligopeptide may be unconstrained, or constrained to a particular conformation by, e.g., the participation of constant cysteine residues in the formation of a constraining disulfide bond.

### *Proteins*

Proteins, like oligopeptides, are composed of a plurality of amino acids, but the term protein is usually reserved for longer peptides, which are able to fold into a stable conformation. A protein may be composed of two or more polypeptide chains, held together by covalent or noncovalent crosslinks. These may occur in a homooligomeric or a heterooligomeric state.

A peptide is considered a protein if it (1) is at least 50 amino acids long, or (2) has at least two stabilizing covalent crosslinks (e.g., disulfide bonds). Thus, conotoxins are considered proteins.

Usually, the proteins of a protein library will be characterizable as having both constant residues (the same



for all proteins in the library) and variable residues (which vary from member to member). This is simply because, for a given range of variation at each position, the sequence space (simple diversity) grows exponentially with the number of residue positions, so at some point it becomes inconvenient for all residues of a peptide to be variable positions. Since proteins are usually larger than oligopeptides, it is more common for protein libraries than oligopeptide libraries to feature variable positions.

In the case of a protein library, it is desirable to focus the mutations at those sites which are tolerant of mutation. These may be determined by alanine scanning mutagenesis or by comparison of the protein sequence to that of homologous proteins of similar activity. It is also more likely that mutation of surface residues will directly affect binding. Surface residues may be determined by inspecting a 3D structure of the protein, or by labeling the surface and then ascertaining which residues have received labels. They may also be inferred by identifying regions of high hydrophilicity within the protein.

Because proteins are often altered at some sites but not others, protein libraries can be considered a special case of the biased peptide library.

There are several reasons that one might screen a protein library instead of an oligopeptide library, including (1) a particular protein, mutated in the library, has the desired activity to some degree already, and (2) the oligopeptides are not expected to have a sufficiently high affinity or specificity since they do not have a stable conformation.

When the protein library is based on a parental protein which does not have the desired activity, the parental protein will usually be one which is of high stability (melting point  $\geq 50$  deg. C.) and/or possessed of hypervariable regions.

The variable domains of an antibody possess

hypervariable regions and hence, in some embodiments, the protein library comprises members which comprise a mutant of VH or VL chain, or a mutant of an antigen-specific binding fragment of such a chain. VH and VL chains are usually each about 110 amino acid residues, and are held in proximity by a disulfide bond between the adjoining CL and CH1 regions to form a variable domain. Together, the VH, VL, CL and CH1 form an Fab fragment.

In human heavy chains, the hypervariable regions are at 31-35, 49-65, 98-111 and 84-88, but only the first three are involved in antigen binding. There is variation among VH and VL chains at residues outside the hypervariable regions, but to a much lesser degree.

A sequence is considered a mutant of a VH or VL chain if it is at least 80% identical to a naturally occurring VH or VL chain at all residues outside the hypervariable region.

In a preferred embodiment, such antibody library members comprise both at least one VH chain and at least one VL chain, at least one of which is a mutant chain, and which chains may be derived from the same or different antibodies. The VH and VL chains may be covalently joined by a suitable linker moiety, as in a "single chain antibody", or they may be noncovalently joined, as in a naturally occurring variable domain.

If the joining is noncovalent, and the library is displayed on cells or virus, then either the VH or the VL chain may be fused to the carrier surface/coat protein. The complementary chain may be co-expressed, or added exogenously to the library.

The members may further comprise some or all of an antibody constant heavy and/or constant light chain, or a mutant thereof.

#### Peptoid Library

A peptoid is an analogue of a peptide in which one or

more of the peptide bonds (-NH-CO-) are replaced by pseudo-peptide bonds, which may be the same or different. It is not necessary that all of the peptide bonds be replaced, i.e., a peptoid may include one or more conventional amino acid residues, e.g., proline.

A peptide bond has two small divalent linker elements, -NH- and -CO-. Thus, a preferred class of pseudo-peptide bonds are those which consist of two small divalent linker elements. Each may be chosen independently from the group consisting of amine (-NH-), substituted amine (-NR-), carbonyl (-CO-), thiocarbonyl (-CS-), methylene (-CH<sub>2</sub>-), monosubstituted methylene (-CHR-), disubstituted methylene (-CR<sub>1</sub>R<sub>2</sub>-), ether (-O-) and thioether (-S-). The more preferred pseudo-peptide bonds include:

N-modified -NRCO-

Carba Ψ -CH<sub>2</sub>-CH<sub>2</sub>-

Depsi Ψ -CO-O-

Hydroxyethylene Ψ -CHOH-CH<sub>2</sub>-

Ketomethylene Ψ -CO-CH<sub>2</sub>-

Methylene-Oxy -CH<sub>2</sub>-O-

Reduced -CH<sub>2</sub>-NH-

Thiomethylene -CH<sub>2</sub>-S-

Thiopeptide -CS-NH-

Retro-Inverso -CO-NH-

A single peptoid molecule may include more than one kind of pseudo-peptide bond.

For the purposes of introducing diversity into a peptoid library, one may vary (1) the side chains attached to the core main chain atoms of the monomers linked by the pseudo-peptide bonds, and/or (2) the side chains (e.g., the R of an -NRCO-) of the pseudo-peptide bonds. Thus, in one embodiment, the monomeric units which are not amino acid residues are of the structure -NR<sub>1</sub>-CR<sub>2</sub>-CO-, where at least one of R<sub>1</sub> and R<sub>2</sub> are not hydrogen. If there is variability in the pseudo-peptide bond, this is most conveniently done by

94

using an -NRCO- or other pseudopeptide bond with an R group, and varying the R group. In this event, the R group will usually be any of the side chains characterizing the amino acids of peptides, as previously discussed.

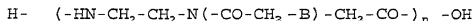
If the R group of the pseudopeptide bond is not variable, it will usually be small, e.g., not more than 10 atoms (e.g., hydroxyl, amino, carboxyl, methyl, ethyl, propyl).

If the conjugation chemistries are compatible, a simple combinatorial library may include both peptides and peptoids.

#### Peptide Nucleic Acid Library

A PNA oligomer is here defined as one comprising a plurality of units, at least one of which is a PNA monomer which comprises a side chain comprising a nucleobase. For nucleobases, see USP 6,077,835.

The classic PNA oligomer is composed of (2-aminoethyl)glycine units, with nucleobases attached by methylene carbonyl linkers. That is, it has the structure



where the outer parenthesized substructure is the PNA monomer.

In this structure, the nucleobase B is separated from the backbone N by three bonds, and the points of attachment of the side chains are separated by six bonds. The nucleobase may be any of the bases included in the nucleotides discussed in connection with oligonucleotide libraries. The bases of nucleotides A, G, T, C and U are preferred.

A PNA oligomer may further comprise one or more amino acid residues, especially glycine and proline.

One can readily envision related molecules in which (1)

the -COCH<sub>2</sub>- linker is replaced by another linker, especially one composed of two small divalent linkers as defined previously, (2) a side chain is attached to one of the three main chain carbons not participating in the peptide bond (either instead or in addition to the side chain attached to the N of the classic PNA); and/or (3) the peptide bonds are replaced by pseudopeptide bonds as disclosed previously in the context of peptoids.

PNA oligomer libraries have been made; see e.g. Cook, 6,204,326.

#### Small Organic Compound Library

The small organic compound library ("compound library", for short) is a combinatorial library whose members are suitable for use as drugs if, indeed, they have the ability to mediate a biological activity of the target protein.

Peptides have certain disadvantages as drugs. These include susceptibility to degradation by serum proteases, and difficulty in penetrating cell membranes. Preferably, all or most of the compounds of the compound library avoid, or at least do not suffer to the same degree, one or more of the pharmaceutical disadvantages of peptides.

In designing a compound library, it is helpful to bear in mind the methods of molecular modification typically used to obtain new drugs. Three basic kinds of modification may be identified: disjunction, in which a lead drug is simplified to identify its component pharmacophoric moieties; conjunction, in which two or more known pharmacophoric moieties, which may be the same or different, are associated, covalently or noncovalently, to form a new drug; and alteration, in which one moiety is replaced by another which may be similar or different, but which is not in effect a disjunction or conjunction. The use of the terms "disjunction", "conjunction" and "alteration" is intended only to connote the structural relationship of the end product to the original leads, and not how the new drugs

are actually synthesized, although it is possible that the two are the same.

The process of disjunction is illustrated by the evolution of neostigmine (1931) and edrophonium (1952) from physostigmine (1925). Subsequent conjunction is illustrated by demecarium (1956) and ambenonium (1956).

Alterations may modify the size, polarity, or electron distribution of an original moiety. Alterations include ring closing or opening, formation of lower or higher homologues, introduction or saturation of double bonds, introduction of optically active centers, introduction, removal or replacement of bulky groups, isosteric or bioisosteric substitution, changes in the position or orientation of a group, introduction of alkylating groups, and introduction, removal or replacement of groups with a view toward inhibiting or promoting inductive (electrostatic) or conjugative (resonance) effects.

Thus, the substituents may include electron acceptors and/or electron donors. Typical electron donors (+I) include  $-CH_3$ ,  $-CH_2R$ ,  $-CHR_2$ ,  $-CR_3$  and  $-COO^-$ . Typical electron acceptors (-I) include  $-NH_3^+$ ,  $-NR_3^+$ ,  $-NO_2$ ,  $-CN$ ,  $-COOH$ ,  $-COOR$ ,  $-CHO$ ,  $-COR$ ,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-OH$ ,  $-OR$ ,  $-SH$ ,  $-SR$ ,  $-CH=CH_2$ ,  $-CR=CR_2$ , and  $-C=CH$ .

The substituents may also include those which increase or decrease electronic density in conjugated systems. The former (+R) groups include  $-CH_3$ ,  $-CR_3$ ,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-OR$ ,  $-OCOR$ ,  $-SH$ ,  $-SR$ ,  $-NH_2$ ,  $-NR_2$ , and  $-NHCOR$ . The later (-R) groups include  $-NO_2$ ,  $-CN$ ,  $-CHC$ ,  $-COR$ ,  $-COOH$ ,  $-COOR$ ,  $-CONH_2$ ,  $-SO_2R$  and  $-CF_3$ .

Synthetically speaking, the modifications may be achieved by a variety of unit processes, including nucleophilic and electrophilic substitution, reduction and oxidation, addition elimination, double bond cleavage, and cyclization.

For the purpose of constructing a library, a compound, or a family of compounds, having one or more pharmacological

activities (which need not be related to the known or suspected activities of the target protein), may be disjoined into two or more known or potential pharmacophoric moieties. Analogues of each of these moieties may be identified, and mixtures of these analogues reacted so as to reassemble compounds which have some similarity to the original lead compound. It is not necessary that all members of the library possess moieties analogous to all of the moieties of the lead compound.

The design of a library may be illustrated by the example of the benzodiazepines. Several benzodiazepine drugs, including chlordiazepoxide, diazepam and oxazepam, have been used as anti-anxiety drugs. Derivatives of benzodiazepines have widespread biological activities; derivatives have been reported to act not only as anxiolytics, but also as anticonvulsants; cholecystokinin (CCK) receptor subtype A or B, kappa opioid receptor, platelet activating factor, and HIV transactivator Tat antagonists, and GPIIb/IIIa, reverse transcriptase and ras farnesyltransferase inhibitors.

The benzodiazepine structure has been disjoined into a 2-aminobenzophenone, an amino acid, and an alkylating agent. See Bunin, et al., Proc. Nat. Acad. Sci. USA, 91:4708 (1994). Since only a few 2-aminobenzophenone derivatives are commercially available, it was later disjoined into 2-aminoarylstannane, an acid chloride, an amino acid, and an alkylating agent. Bunin, et al., Meth. Enzymol., 267:448 (1996). The arylstannane may be considered the core structure upon which the other moieties are substituted, or all four may be considered equals which are conjoined to make each library member.

A basic library synthesis plan and member structure is shown in Figure 1 of Fowlkes, et al., U.S. Serial No. 08/740,671, incorporated by reference in its entirety. The acid chloride building block introduces variability at the R<sup>1</sup> site. The R<sup>2</sup> site is introduced by the amino acid, and the

R<sup>1</sup> site by the alkylating agent. The R<sup>4</sup> site is inherent in the arylstannane. Bunin, et al. generated a 1, 4-benzodiazepine library of 11,200 different derivatives prepared from 20 acid chlorides, 35 amino acids, and 16 alkylating agents. (No diversity was introduced at R<sup>4</sup>; this group was used to couple the molecule to a solid phase.) According to the Available Chemicals Directory (HDL Information Systems, San Leandro CA), over 300 acid chlorides, 80 Fmoc-protected amino acids and 800 alkylating agents were available for purchase (and more, of course, could be synthesized). The particular moieties used were chosen to maximize structural dispersion, while limiting the numbers to those conveniently synthesized in the wells of a microtiter plate. In choosing between structurally similar compounds, preference was given to the least substituted compound.

The variable elements included both aliphatic and aromatic groups. Among the aliphatic groups, both acyclic and cyclic (mono- or poly-) structures, substituted or not, were tested. (While all of the acyclic groups were linear, it would have been feasible to introduce a branched aliphatic). The aromatic groups featured either single and multiple rings, fused or not, substituted or not, and with heteroatoms or not. The secondary substituents included -NH<sub>2</sub>, -OH, -OMe, -CN, -Cl, -F, and -COOH. While not used, spacer moieties, such as -O-, -S-, -OO-, -CS-, -NH-, and -NR-, could have been incorporated.

Bunin et al. suggest that instead of using a 1, 4-benzodiazepine as a core structure, one may instead use a 1, 4-benzodiazepine-2, 5-dione structure.

As noted by Bunin et al., it is advantageous, although not necessary, to use a linking strategy which leaves no trace of the linking functionality, as this permits construction of a more diverse library.

Other combinatorial nonoligomeric compound libraries known or suggested in the art have been based on carbamates,



mercaptoacylated pyrrolidines, phenolic agents, aminimides, N-acylamino ethers (made from amino alcohols, aromatic hydroxy acids, and carboxylic acids), N-alkylamino ethers (made from aromatic hydroxy acids, amino alcohols and aldehydes) 1, 4-piperazines, and 1, 4-piperazine-6-ones.

DeWitt, et al., Proc. Nat. Acad. Sci. (USA), 90:6909-13 (1993) describe the simultaneous but separate, synthesis of 40 discrete hydantoins and 40 discrete benzodiazepines. They carry out their synthesis on a solid support (inside a gas dispersion tube), in an array format, as opposed to other conventional simultaneous synthesis techniques (e.g., in a well, or on a pin). The hydantoins were synthesized by first simultaneously deprotecting and then treating each of five amino acid resins with each of eight isocyanates. The benzodiazepines were synthesized by treating each of five deprotected amino acid resins with each of eight 2-amino benzophenone imines.

Chen, et al., J. Am. Chem. Soc., 116:2661-62 (1994) described the preparation of a pilot (9 member) combinatorial library of formate esters. A polymer bead-bound aldehyde preparation was "split" into three aliquots, each reacted with one of three different ylide reagents. The reaction products were combined, and then divided into three new aliquots, each of which was reacted with a different Michael donor. Compound identity was found to be determinable on a single bead basis by gas chromatography/mass spectroscopy analysis.

Holmes, USP 5,549,974 (1996) sets forth methodologies for the combinatorial synthesis of libraries of thiazolidinones and metathiazanones. These libraries are made by combination of amines, carbonyl compounds, and thiols under cyclization conditions.

Ellman, USP 5,545,568 (1996) describes combinatorial synthesis of benzodiazepines, prostaglandins, beta-turn mimetics, and glycerol-based compounds. See also Ellman, USP 5,288,514.

Summerton, USP 5,506,337 (1996) discloses methods of preparing a combinatorial library formed predominantly of morpholino subunit structures.

Heterocyclic combinatorial libraries are reviewed generally in Nefzi, et al., Chem. Rev., 97:449-472 (1997).

For pharmacological classes, see, e.g., Goth, Medical Pharmacology: Principles and Concepts (C.V. Mosby Co.: 8th ed. 1976); Korolkovas and Burckhalter, Essentials of Medicinal Chemistry (John Wiley & Sons, Inc.: 1976). For synthetic methods, see, e.g., Warren, Organic Synthesis: The Disconnection Approach (John Wiley & Sons, Ltd.: 1982); Fuson, Reactions of Organic Compounds (John Wiley & Sons: 1966); Payne and Payne, How to do an Organic Synthesis (Allyn and Bacon, Inc.: 1969); Greene, Protective Groups in Organic Synthesis (Wiley-Interscience). For selection of substituents, see e.g., Hansch and Leo, Substituent Constants for Correlation Analysis in Chemistry and Biology (John Wiley & Sons: 1979).

The library is preferably synthesized so that the individual members remain identifiable so that, if a member is shown to be active, it is not necessary to analyze it. Several methods of identification have been proposed, including:

- (1) encoding, i.e., the attachment to each member of an identifier moiety which is more readily identified than the member proper. This has the disadvantage that the tag may itself influence the activity of the conjugate.
- (2) spatial addressing, e.g., each member is synthesized only at a particular coordinate on or in a matrix, or in a particular chamber. This might be, for example, the location of a particular pin, or a particular well on a microtiter plate, or inside a "tea bag".

The present invention is not limited to any particular form

of identification.

However, it is possible to simply characterize those members of the library which are found to be active, based on the characteristic spectroscopic indicia of the various building blocks.

Solid phase synthesis permits greater control over which derivatives are formed. However, the solid phase could interfere with activity. To overcome this problem, some or all of the molecules of each member could be liberated, after synthesis but before screening.

Examples of candidate simple libraries which might be evaluated include derivatives of the following:

Cyclic Compounds Containing One Hetero Atom

Heteronitrogen

pyrroles  
pentasubstituted pyrroles  
pyrrolidines  
pyrrolines  
prolines  
indoles  
beta-carbolines  
pyridines  
dihydropyridines  
1,4-dihydropyridines  
pyrido[2,3-d]pyrimidines  
tetrahydro-3H-imidazo[4,5-c] pyridines  
Isoquinolines  
tetrahydroisoquinolines  
quinolones  
beta-lactams  
azabicyclo[4.3.0]nonen-8-one amino acid  
Heterooxygen  
furans  
tetrahydrofurans  
2,5-disubstituted tetrahydrofurans  
pyrans

102

hydroxypyranones

tetrahydroxypyranones

gamma-butyrolactones

Heterosulfur

sulfolenes

Cyclic Compounds with Two or More Hetero atoms

Multiple heteronitrogens

imidazoles

pyrazoles

piperazines

diketopiperazines

arylpiperazines

benzylpiperazines

benzodiazepines

1,4-benzodiazepine-2,5-diones

hydantoins

5-alkoxyhydantoins

dihydropyrimidines

1,3-disubstituted-5,6-dihydropyrimidine-2,4-diones

cyclic ureas

cyclic thioureas

quinazolines

chiral 3-substituted-quinazoline-2,4-diones

triazoles

1,2,3-triazoles

purines

Heteronitrogen and Heterooxygen

dikelomorpholines

isoxazoles

isoxazolines

Heteronitrogen and Heterosulfur

thiazolidines

N-axylthiazolidines

103

dihydrothiazoles

2-methylene-2,3-dihydrothiazates

2-aminothiazoles

thiophenes

3-amino thiophenes

4-thiazolidinones

4-melathiazanones

benzisothiazolones

For details on synthesis of libraries, see Nefzi, et al., Chem. Rev., 97:449-72 (1997), and references cited therein.

#### Pharmaceutical Methods and Preparations

The preferred animal subject of the present invention is a mammal. By the term "mammal" is meant an individual belonging to the class Mammalia. The invention is particularly useful in the treatment of human subjects, although it is intended for veterinary and nutritional uses as well. Preferred nonhuman subjects are of the orders Primata (e.g., apes and monkeys), Artiodactyla or Perissodactyla (e.g., cows, pigs, sheep, horses, goats), Carnivora (e.g., cats, dogs), Rodenta (e.g., rats, mice, guinea pigs, hamsters), Lagomorpha (e.g., rabbits) or other pet, farm or laboratory mammals.

The term "protection", as used herein, is intended to include "prevention," "suppression" and "treatment." "Prevention", strictly speaking, involves administration of the pharmaceutical prior to the induction of the disease (or other adverse clinical condition). "Suppression" involves administration of the composition prior to the clinical appearance of the disease. "Treatment" involves administration of the protective composition after the appearance of the disease.

It will be understood that in human and veterinary medicine, it is not always possible to distinguish between "preventing" and "suppressing" since the ultimate inductive

event or events may be unknown, latent, or the patient is not ascertained until well after the occurrence of the event or events. Therefore, unless qualified, the term "prevention" will be understood to refer to both prevention in the strict sense, and to suppression.

The preventative or prophylactic use of a pharmaceutical usually involves identifying subjects who are at higher risk than the general population of contracting the disease, and administering the pharmaceutical to them in advance of the clinical appearance of the disease. The effectiveness of such use is measured by comparing the subsequent incidence or severity of the disease, or of particular symptoms of the disease, in the treated subjects against that in untreated subjects of the same high risk group.

While high risk factors vary from disease to disease, in general, these include (1) prior occurrence of the disease in one or more members of the same family, or, in the case of a contagious disease, in individuals with whom the subject has come into potentially contagious contact at a time when the earlier victim was likely to be contagious, (2) a prior occurrence of the disease in the subject, (3) prior occurrence of a related disease, or a condition known to increase the likelihood of the disease, in the subject; (4) appearance of a suspicious level of a marker of the disease, or a related disease or condition; (5) a subject who is immunologically compromised, e.g., by radiation treatment, HIV infection, drug use, etc., or (6) membership in a particular group (e.g., a particular age, sex, race, ethnic group, etc.) which has been epidemiologically associated with that disease.

In some cases, it may be desirable to provide prophylaxis for the general population, and not just a high risk group. This is most likely to be the case when essentially all are at risk of contracting the disease, the effects of the disease are serious, the therapeutic index of

the prophylactic agent is high, and the cost of the agent is low.

A prophylaxis or treatment may be curative, that is, directed at the underlying cause of a disease, or ameliorative, that is, directed at the symptoms of the disease, especially those which reduce the quality of life.

It should also be understood that to be useful, the protection provided need not be absolute, provided that it is sufficient to carry clinical value. An agent which provides protection to a lesser degree than do competitive agents may still be of value if the other agents are ineffective for a particular individual, if it can be used in combination with other agents to enhance the level of protection, or if it is safer than competitive agents. It is desirable that there be a statistically significant ( $p=0.05$  or less) improvement in the treated subject relative to an appropriate untreated control, and it is desirable that this improvement be at least 10%, more preferably at least 25%, still more preferably at least 50%, even more preferably at least 100%, in some indicia of the incidence or severity of the disease or of at least one symptom of the disease.

At least one of the drugs of the present invention may be administered, by any means that achieve their intended purpose, to protect a subject against a disease or other adverse condition. The form of administration may be systemic or topical. For example, administration of such a composition may be by various parenteral routes such as subcutaneous, intravenous, intradermal, intramuscular, intraperitoneal, intranasal, transdermal, or buccal routes. Alternatively, or concurrently, administration may be by the oral route. Parenteral administration can be by bolus injection or by gradual perfusion over time.

A typical regimen comprises administration of an effective amount of the drug, administered over a period ranging from a single dose, to dosing over a period of hours, days, weeks, months, or years.

It is understood that the suitable dosage of a drug of the present invention will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired. However, the most preferred dosage can be tailored to the individual subject, as is understood and determinable by one of skill in the art, without undue experimentation. This will typically involve adjustment of a standard dose, e.g., reduction of the dose if the patient has a low body weight.

Prior to use in humans, a drug will first be evaluated for safety and efficacy in laboratory animals. In human clinical studies, one would begin with a dose expected to be safe in humans, based on the preclinical data for the drug in question, and on customary doses for analogous drugs (if any). If this dose is effective, the dosage may be decreased, to determine the minimum effective dose, if desired. If this dose is ineffective, it will be cautiously increased, with the patients monitored for signs of side effects. See, e.g., Berkow et al, eds., *The Merck Manual*, 15th edition, Merck and Co., Rahway, N.J., 1987; Goodman et al., eds., *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 8th edition, Pergamon Press, Inc., Elmsford, N.Y., (1990); Avery's *Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics*, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987), Ebadi, *Pharmacology*, Little, Brown and Co., Boston, (1985), which references and references cited therein, are entirely incorporated herein by reference.

The total dose required for each treatment may be administered by multiple doses or in a single dose. The protein may be administered alone or in conjunction with other therapeutics directed to the disease or directed to other symptoms thereof.

Typical pharmaceutical doses, for adult humans, are in the range of 1 ng to 10g per day, more often 1 mg to 1g per



day.

The appropriate dosage form will depend on the disease, the pharmaceutical, and the mode of administration; possibilities include tablets, capsules, lozenges, dental pastes, suppositories, inhalants, solutions, ointments and parenteral depots. See, e.g., Berker, *supra*, Goodman, *supra*, Avery, *supra* and Ebadi, *supra*, which are entirely incorporated herein by reference, including all references cited therein.

In the case of peptide drugs, the drug may be administered in the form of an expression vector comprising a nucleic acid encoding the peptide; such a vector, after incorporation into the genetic complement of a cell of the patient, directs synthesis of the peptide. Suitable vectors include genetically engineered poxviruses (vaccinia), adenoviruses, adeno-associated viruses, herpesviruses and lentiviruses which are or have been rendered nonpathogenic.

In addition to at least one drug as described herein, a pharmaceutical composition may contain suitable pharmaceutically acceptable carriers, such as excipients, carriers and/or auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. See, e.g., Berker, *supra*, Goodman, *supra*, Avery, *supra* and Ebadi, *supra*, which are entirely incorporated herein by reference, included all references cited therein.

## Assay Compositions and Methods

### Target Organism

The invention contemplates that it may be appropriate to ascertain or to mediate the biological activity of a substance of this invention in a target organism.

The target organism may be a plant, animal, or microorganism.

In the case of a plant, it may be an economic plant, in which case the drug may be intended to increase the disease,

weather or pest resistance, alter the growth characteristics, or otherwise improve the useful characteristics or mute undesirable characteristics of the plant. Or it may be a weed, in which case the drug may be intended to kill or otherwise inhibit the growth of the plant, or to alter its characteristics to convert it from a weed to an economic plant. The plant may be a tree, shrub, crop, grass, etc. The plant may be an algae (which are in some cases also microorganisms), or a vascular plant, especially gymnosperms (particularly conifers) and angiosperms. Angiosperms may be monocots or dicots. The plants of greatest interest are rice, wheat, corn, alfalfa, soybeans, potatoes, peanuts, tomatoes, melons, apples, pears, plums, pineapples, fir, spruce, pine, cedar, and oak.

If the target organism is a microorganism, it may be algae, bacteria, fungi, or a virus (although the biological activity of a virus must be determined in a virus-infected cell). The microorganism may be human or other animal or plant pathogen, or it may be nonpathogenic. It may be a soil or water organism, or one which normally lives inside other living things.

If the target organism is an animal, it may be a vertebrate or a nonvertebrate animal. Nonvertebrate animals are chiefly of interest when they act as pathogens or parasites, and the drugs are intended to act as biocidal or biostatic agents. Nonvertebrate animals of interest include worms, mollusks, and arthropods.

The target organism may also be a vertebrate animal, i.e., a mammal, bird, reptile, fish or amphibian. Among mammals, the target animal preferably belongs to the order Primata (humans, apes and monkeys), Artiodactyla (e.g., cows, pigs, sheep, goats, horses), Rodenta (e.g., mice, rats) Lagomorpha (e.g., rabbits, hares), or Carnivora (e.g., cats, dogs). Among birds, the target animals are preferably of the orders Anseriformes (e.g., ducks, geese, swans) or Galliformes (e.g., quails, grouse, pheasants, turkeys and

chickens). Among fish, the target animal is preferably of the order Clupeiformes (e.g., sardines, shad, anchovies, whitefish, salmon).

### 5 Target Tissues

The term "target tissue" refers to any whole animal, physiological system, whole organ, part of organ, miscellaneous tissue, cell, or cell component (e.g., the cell membrane) of a target animal in which biological  
0 activity may be measured.

Routinely in mammals one would choose to compare and contrast the biological impact on virtually any and all tissues which express the subject receptor protein. The main tissues to use are: brain, heart, lung, kidney, liver, pancreas, skin, intestines, adipose, stomach, skeletal  
3 muscle, adrenal glands, breast, prostate, vasculature, retina, cornea, thyroid gland, parathyroid glands, thymus, bone marrow, bone, etc.

Another classification would be by cell type: B cells, T cells, macrophages, neutrophils, eosinophils, mast cells, platelets, megakaryocytes, erythrocytes, bone marrow stomal  
6 cells, fibroblasts, neurons, astrocytes, neuroglia, microglia, epithelial cells (from any organ, e.g. skin, breast, prostate, lung, intestines etc), cardiac muscle cells, smooth muscle cells, striated muscle cells, osteoblasts, osteocytes, chondroblasts, chondrocytes, keratinocytes, melanocytes, etc.

Of course, in the case of a unicellular organism, there is no distinction between the "target organism" and the "target tissue".

### Screening Assays

Assays intended to determine the binding or the biological activity of a substance are called preliminary screening assays.

Screening assays will typically be either in vitro

110

(cell-free) assays (for binding to an immobilized receptor) or cell-based assays (for alterations in the phenotype of the cell). They will not involve screening of whole multicellular organisms, or isolated organs. The comments on diagnostic biological assays apply mutatis mutandis to screening cell-based assays.

#### In Vitro vs. In Vivo Assays

The term *in vivo* is descriptive of an event, such as binding or enzymatic action, which occurs within a living organism. The organism in question may, however, be genetically modified. The term *in vitro* refers to an event which occurs outside a living organism. Parts of an organism (e.g., a membrane, or an isolated biochemical) are used, together with artificial substrates and/or conditions. For the purpose of the present invention, the term *in vitro* excludes events occurring inside or on an intact cell, whether of a unicellular or multicellular organism.

*In vivo* assays include both cell-based assays, and organismic assays. The cell-based assays include both assays on unicellular organisms, and assays on isolated cells or cell cultures derived from multicellular organisms. The cell cultures may be mixed, provided that they are not organized into tissues or organs. The term organismic assay refers to assays on whole multicellular organisms, and assays on isolated organs or tissues of such organisms.

#### In vitro Diagnostic Methods and Reagents

The *in vitro* assays of the present invention may be applied to any suitable analyte-containing sample, and may be qualitative or quantitative in nature.

#### Sample

The sample will normally be a biological fluid, such as blood, urine, lymph, semen, milk, or cerebrospinal fluid, or

111

a fraction or derivative thereof, or a biological tissue, in the form of, e.g., a tissue section or homogenate. However, the sample conceivably could be (or derived from) a food or beverage, a pharmaceutical or diagnostic composition, soil, or surface or ground water. If a biological fluid or tissue, it may be taken from a human or other mammal, vertebrate or animal, or from a plant. The preferred sample is blood, or a fraction or derivative thereof.

### *Binding and Reaction Assays*

The assay may be a binding assay, in which one step involves the binding of a diagnostic reagent to the analyte, or a reaction assay, which involves the reaction of a reagent with the analyte. The reagents used in a binding assay may be classified as to the nature of their interaction with analyte: (1) analyte analogues, or (2) analyte binding molecules (ABM). They may be labeled or insolubilized.

In a reaction assay, the assay may look for a direct reaction between the analyte and a reagent which is reactive with the analyte, or if the analyte is an enzyme or enzyme inhibitor, for a reaction catalyzed or inhibited by the analyte. The reagent may be a reactant, a catalyst, or an inhibitor for the reaction.

An assay may involve a cascade of steps in which the product of one step acts as the target for the next step. These steps may be binding steps, reaction steps, or a combination thereof.

### *Signal Producing System (SPS)*

In order to detect the presence, or measure the amount, of an analyte, the assay must provide for a signal producing system (SPS) in which there is a detectable difference in the signal produced, depending on whether the analyte is present or absent (or, in a quantitative assay, on the

112

amount of the analyte). The detectable signal may be one which is visually detectable, or one detectable only with instruments. Possible signals include production of colored or luminescent products, alteration of the characteristics (including amplitude or polarization) of absorption or emission of radiation by an assay component or product, and precipitation or agglutination of a component or product. The term "signal" is intended to include the discontinuance of an existing signal, or a change in the rate of change of an observable parameter, rather than a change in its absolute value. The signal may be monitored manually or automatically.

In a reaction assay, the signal is often a product of the reaction. In a binding assay, it is normally provided by a label borne by a labeled reagent.

#### Labels

The component of the signal producing system which is most intimately associated with the diagnostic reagent is called the "label". A label may be, e.g., a radioisotope, a fluorophore, an enzyme, a co-enzyme, an enzyme substrate, an electron-dense compound, an agglutinable particle.

The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography. Isotopes which are particularly useful for the purpose of the present invention include  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$  and  $^{33}\text{P}$ .  $^{125}\text{I}$  is preferred for antibody labeling.

The label may also be a fluorophore. When the fluorescently labeled reagent is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthalaldehyde and fluorescamine.

Alternatively, fluorescence-emitting metals such as

<sup>125</sup>Eu, or others of the lanthanide series, may be incorporated into a diagnostic reagent using such metal chelating groups as diethylenetriaminepentaacetic acid (DTPA) of ethylenediamine-tetraacetic acid (EDTA).

The label may also be a chemiluminescent compound. The presence of the chemiluminescently labeled reagent is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of particularly useful chemiluminescent labeling compounds are luminol, isolumino, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used for labeling. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Enzyme labels, such as horseradish peroxidase and alkaline phosphatase, are preferred. When an enzyme label is used, the signal producing system must also include a substrate for the enzyme. If the enzymatic reaction product is not itself detectable, the SPS will include one or more additional reactants so that a detectable product appears.

An enzyme analyte may act as its own label if an enzyme inhibitor is used as a diagnostic reagent.

#### *Binding Assay Formats*

Binding assays may be divided into two basic types, heterogeneous and homogeneous. In heterogeneous assays, the interaction between the affinity molecule and the analyte does not affect the label, hence, to determine the amount or presence of analyte, bound label must be separated from free label. In homogeneous assays, the interaction does affect the activity of the label, and therefore analyte levels can

114

be deduced without the need for a separation step.

In one embodiment, the ABM is insolubilized by coupling it to a macromolecular support, and analyte in the sample is allowed to compete with a known quantity of a labeled or specifically labelable analyte analogue. The "analyte analogue" is a molecule capable of competing with analyte for binding to the ABM, and the term is intended to include analyte itself. It may be labeled already, or it may be labeled subsequently by specifically binding the label to a moiety differentiating the analyte analogue from analyte. The solid and liquid phases are separated, and the labeled analyte analogue in one phase is quantified. The higher the level of analyte analogue in the solid phase, i.e., sticking to the ABM, the lower the level of analyte in the sample.

In a "sandwich assay", both an insolubilized ABM, and a labeled ABM are employed. The analyte is captured by the insolubilized ABM and is tagged by the labeled ABM, forming a ternary complex. The reagents may be added to the sample in either order, or simultaneously. The ABMs may be the same or different. The amount of labeled ABM in the ternary complex is directly proportional to the amount of analyte in the sample.

The two embodiments described above are both heterogeneous assays. However, homogeneous assays are conceivable. The key is that the label be affected by whether or not the complex is formed.

#### Conjugation Methods

A label may be conjugated, directly or indirectly (e.g., through a labeled anti-ABM antibody), covalently (e.g., with SPDP) or noncovalently, to the ABM, to produce a diagnostic reagent. Similarly, the ABM may be conjugated to a solid phase support to form a solid phase ("capture") diagnostic reagent.

Suitable supports include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases,



natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention.

The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to its target. Thus the support configuration may be spherical, as in a bead, or cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc.

### Biological Assays

A biological assay measures or detects a biological response of a biological entity to a substance.

The biological entity may be a whole organism, an isolated organ or tissue, freshly isolated cells, an immortalized cell line, or a subcellular component (such as a membrane; this term should not be construed as including an isolated receptor). The entity may be, or may be derived from, an organism which occurs in nature, or which is modified in some way. Modifications may be genetic (including radiation and chemical mutants, and genetic engineering) or somatic (e.g., surgical, chemical, etc.). In the case of a multicellular entity, the modifications may affect some or all cells. The entity need not be the target organism, or a derivative thereof, if there is a reasonable correlation between bioassay activity in the assay entity and biological activity in the target organism.

The entity is placed in a particular environment, which may be more or less natural. For example, a culture medium may, but need not, contain serum or serum substitutes, and it may, but need not, include a support matrix of some kind, it may be still, or agitated. It may contain particular biological or chemical agents, or have particular physical parameters (e.g., temperature), that are intended to nourish

or challenge the biological entity.

There must also be a detectable biological marker for the response. At the cellular level, the most common markers are cell survival and proliferation, cell behavior (clustering, motility), cell morphology (shape, color), and biochemical activity (overall DNA synthesis, overall protein synthesis, and specific metabolic activities, such as utilization of particular nutrients, e.g., consumption of oxygen, production of CO<sub>2</sub>, production of organic acids, uptake or discharge of ions).

The direct signal produced by the biological marker may be transformed by a signal producing system into a different signal which is more observable, for example, a fluorescent or colorimetric signal.

The entity, environment, marker and signal producing system are chosen to achieve a clinically acceptable level of sensitivity, specificity and accuracy.

In some cases, the goal will be to identify substances which mediate the biological activity of a natural biological entity, and the assay is carried out directly with that entity. In other cases, the biological entity is used simply as a model of some more complex (or otherwise inconvenient to work with) biological entity. In that event, the model biological entity is used because activity in the model system is considered more predictive of activity in the ultimate natural biological entity than is simple binding activity in an in vitro system. The model entity is used instead of the ultimate entity because the former is more expensive or slower to work with, or because ethical considerations forbid working with the ultimate entity yet.

The model entity may be naturally occurring, if the model entity usefully models the ultimate entity under some conditions. Or it may be non-naturally occurring, with modifications that increase its resemblance to the ultimate entity.

117

Transgenic animals, such as transgenic mice, rats, and rabbits, have been found useful as model systems.

In cell-based model assays, where the biological activity is mediated by binding to a receptor (target protein), the receptor may be functionally connected to a signal (biological marker) producing system, which may be endogenous or exogenous to the cell.

There are a number of techniques of doing this.

#### "Zero-Hybrid" Systems

In these systems, the binding of a peptide to the target protein results in a screenable or selectable phenotypic change, without resort to fusing the target protein (or a ligand binding moiety thereof) to an endogenous protein. It may be that the target protein is endogenous to the host cell, or is substantially identical to an endogenous receptor so that it can take advantage of the latter's native signal transduction pathway. Or sufficient elements of the signal transduction pathway normally associated with the target protein may be engineered into the cell so that the cell signals binding to the target protein.

#### "One-Hybrid" Systems

In these systems, a chimera receptor, a hybrid of the target protein and an endogenous receptor, is used. The chimeric receptor has the ligand binding characteristics of the target protein and the signal transduction characteristics of the endogenous receptor. Thus, the normal signal transduction pathway of the endogenous receptor is subverted.

Preferably, the endogenous receptor is inactivated, or the conditions of the assay avoid activation of the endogenous receptor, to improve the signal-to-noise ratio.

See Fowlkes USP 5,789,184 for a yeast system.

Another type of "one-hybrid" system combines a peptide:

DNA-binding domain fusion with an unfused target receptor that possesses an activation domain.

#### "Two-Hybrid" System

In a preferred embodiment, the cell-based assay is a two hybrid system. This term implies that the ligand is incorporated into a first hybrid protein, and the receptor into a second hybrid protein. The first hybrid also comprises component A of a signal generating system, and the second hybrid comprises component B of that system. Components A and B, by themselves, are insufficient to generate a signal. However, if the ligand binds the receptor, components A and B are brought into sufficiently close proximity so that they can cooperate to generate a signal.

Components A and B may naturally occur, or be substantially identical to moieties which naturally occur, as components of a single naturally occurring biomolecule, or they may naturally occur, or be substantially identical to moieties which naturally occur, as separate naturally occurring biomolecules which interact in nature.

#### Two-Hybrid System: Transcription Factor Type

In a preferred "two-hybrid" embodiment, one member of a peptide ligand:receptor binding pair is expressed as a fusion to a DNA-binding domain (DBD) from a transcription factor (this fusion protein is called the "bait"), and the other is expressed as a fusion to a transactivation domain (TAD) (this fusion protein is called the "fish", the "prey", or the "catch"). The transactivation domain should be complementary to the DNA-binding domain, i.e., it should interact with the latter so as to activate transcription of a specially designed reporter gene that carries a binding site for the DNA-binding domain. Naturally, the two fusion proteins must likewise be complementary.

This complementarity may be achieved by use of the

complementary and separable DNA-binding and transcriptional activator domains of a single transcriptional activator protein, or one may use complementary domains derived from different proteins. The domains may be identical to the native domains, or mutants thereof. The assay members may be fused directly to the DBD or TAD, or fused through an intermediated linker.

The target DNA operator may be the native operator sequence, or a mutant operator. Mutations in the operator may be coordinated with mutations in the DBD and the TAD. An example of a suitable transcription activation system is one comprising the DNA-binding domain from the bacterial repressor LexA and the activation domain from the yeast transcription factor Gal4, with the reporter gene operably linked to the LexA operator.

It is not necessary to employ the intact target receptor; just the ligand-binding moiety is sufficient.

The two fusion proteins may be expressed from the same or different vectors. Likewise, the activatable reporter gene may be expressed from the same vector as either fusion protein (or both proteins), or from a third vector.

Potential DNA-binding domains include Gal4, LexA, and mutant domains substantially identical to the above.

Potential activation domains include E. coli B42, Gal4 activation domain II, and HSV VP16, and mutant domains substantially identical to the above.

Potential operators include the native operators for the desired activation domain, and mutant domains substantially identical to the native operator.

The fusion proteins may comprise nuclear localization signals.

The assay system will include a signal producing system, too. The first element of this system is a reporter gene operably linked to an operator responsive to the DBD and TAD of choice. The expression of this reporter gene will result, directly or indirectly, in a selectable or

120

screenable phenotype (the signal). The signal producing system may include, besides the reporter gene, additional genetic or biochemical elements which cooperate in the production of the signal. Such an element could be, for example, a selective agent in the cell growth medium. There may be more than one signal producing system, and the system may include more than one reporter gene.

The sensitivity of the system may be adjusted by, e.g., use of competitive inhibitors of any step in the activation or signal production process, increasing or decreasing the number of operators, using a stronger or weaker DBD or TAD, etc.

When the signal is the death or survival of the cell in question, or proliferation or nonproliferation of the cell in question, the assay is said to be a selection. When the signal merely results in a detectable phenotype by which the signaling cell may be differentiated from the same cell in a nonsignaling state (either way being a living cell), the assay is a screen. However, the term "screening assay" may be used in a broader sense to include a selection. When the narrower sense is intended, we will use the term "nonselective screen".

Various screening and selection systems are discussed in Ladner, USP 5,198,346.

Screening and selection may be for or against the peptide: target protein or compound:target protein interaction.

Preferred assay cells are microbial (bacterial, yeast, algal, protozoal), invertebrate, vertebrate (esp. mammalian, particularly human). The best developed two-hybrid assays are yeast and mammalian systems.

Normally, two hybrid assays are used to determine whether a protein X and a protein Y interact, by virtue of their ability to reconstitute the interaction of the DBD and the TAD. However, augmented two-hybrid assays have been used to detect interactions that depend on a third, non-

protein ligand.

For more guidance on two-hybrid assays, see Brent and Finley, Jr., *Ann. Rev. Genet.*, 31:663-704 (1997); Fremont-Racine, et al., *Nature Genetics*, 277-281 (16 July 1997); Allen, et al., *TIBS*, 511-16 (Dec. 1995); LeCrenier, et al., *BioEssays*, 20:1-6 (1998); Xu, et al., *Proc. Nat. Acad. sci. (USA)*, 94:12473-8 (Nov. 1992); Esotak, et al., *Mol. Cell. Biol.*, 15:5820-9 (1995); Yang, et al., *Nucleic Acids Res.*, 23:1152-6 (1995); Bendixen, et al., *Nucleic Acids Res.*, 22:1778-9 (1994); Fuller, et al., *BioTechniques*, 25:85-92 (July 1998); Cohen, et al., *PNAS (USA)* 95:14272-7 (1998); Kolonin and Finley, Jr., *PNAS (USA)* 95:14266-71 (1998). See also Vasavada, et al., *PNAS (USA)*, 88:10686-90 (1991) (contingent replication assay), and Rehrauer, et al., *J. Biol. Chem.*, 271:23865-73 (1996) (LexA repressor cleavage assay).

#### Two-Hybrid Systems: reporter Enzyme type

In another embodiment, the components A and B reconstitute an enzyme which is not a transcription factor.

As in the last example, the effect of the reconstitution of the enzyme is a phenotypic change which may be a screenable change, a selectable change, or both.

#### In vivo Diagnostic Uses

Radio-labeled ABM may be administered to the human or animal subject. Administration is typically by injection, e.g., intravenous or arterial or other means of administration in a quantity sufficient to permit subsequent dynamic and/or static imaging using suitable radio-detecting devices. The dosage is the smallest amount capable of providing a diagnostically effective image, and may be determined by means conventional in the art, using known radio-imaging agents as a guide.

Typically, the imaging is carried out on the whole body

of the subject, or on that portion of the body or organ relevant to the condition or disease under study. The amount of radio-labeled ABM accumulated at a given point in time in relevant target organs can then be quantified.

A particularly suitable radio-detecting device is a scintillation camera, such as a gamma camera. A scintillation camera is a stationary device that can be used to image distribution of radio-labeled ABM. The detection device in the camera senses the radioactive decay, the distribution of which can be recorded. Data produced by the imaging system can be digitized. The digitized information can be analyzed over time discontinuously or continuously. The digitized data can be processed to produce images, called frames, of the pattern of uptake of the radio-labeled ABM in the target organ at a discrete point in time. In most continuous (dynamic) studies, quantitative data is obtained by observing changes in distributions of radioactive decay in target organs over time. In other words, a time-activity analysis of the data will illustrate uptake through clearance of the radio-labeled binding protein by the target organs with time.

Various factors should be taken into consideration in selecting an appropriate radioisotope. The radioisotope must be selected with a view to obtaining good quality resolution upon imaging, should be safe for diagnostic use in humans and animals, and should preferably have a short physical half-life so as to decrease the amount of radiation received by the body. The radioisotope used should preferably be pharmacologically inert, and, in the quantities administered, should not have any substantial physiological effect.

The ABM may be radio-labeled with different isotopes of iodine, for example  $^{123}\text{I}$ ,  $^{125}\text{I}$ , or  $^{131}\text{I}$  (see for example, U.S. Patent 4,609,725). The extent of radio-labeling must, however be monitored, since it will affect the calculations made based on the imaging results (i.e. a diiodinated ABM



123

will result in twice the radiation count of a similar monoiodinated ABM over the same time frame).

In applications to human subjects, it may be desirable to use radioisotopes other than  $^{125}\text{I}$  for labeling in order to decrease the total dosimetry exposure of the human body and to optimize the detectability of the labeled molecule (though this radioisotope can be used if circumstances require). Ready availability for clinical use is also a factor. Accordingly, for human applications, preferred radio-labels are for example,  $^{99\text{m}}\text{Tc}$ ,  $^{67}\text{Ga}$ ,  $^{68}\text{Ga}$ ,  $^{90}\text{Y}$ ,  $^{111}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{123}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$  or  $^{211}\text{At}$ .

The radio-labeled ABM may be prepared by various methods. These include radio-halogenation by the chloramine - T method or the lactoperoxidase method and subsequent purification by HPLC (high pressure liquid chromatography), for example as described by J. Gutkowska et al in "Endocrinology and Metabolism Clinics of America: (1987) 16 (1):183. Other known methods of radio-labeling can be used, such as IODOBEADS™.

There are a number of different methods of delivering the radio-labeled ABM to the end-user. It may be administered by any means that enables the active agent to reach the agent's site of action in the body of a mammal. Because proteins are subject to being digested when administered orally, parenteral administration, i.e., intravenous, subcutaneous, intramuscular, would ordinarily be used to optimize absorption of an ABM, such as an antibody, which is a protein.

## EXAMPLES

### Example 1

Differentially expressed mouse genes, and corresponding human genes/proteins, were identified as described in this Example, and compiled into Master Table 1.

**Animal Models** Upon separation from their mothers (weaning), C57Bl/6J mice (i.e., C57Bl/6 mice developed by Jackson Labs) were placed on a normal diet (PMI Nutrition International Inc., Brentwood, MO, Prolab RMH3000). Mice were sacrificed at an average of 35, 49, 56, 77, 118, 133, 207, 403, 558 and 725 days of age.

### RNA isolation.

Total RNA was isolated from livers using the RNA STAT-60 Total RNA/mRNA Isolation Reagent according to the manufacturer's instructions (Tel-Test, Friendswood, TX).

### Sample Quantification and Quality Assessment

Total RNA was quantified and assessed for quality on a Bioanalyzer RNA 6000 Nano chip (Agilent). Each chip contained an interconnected set of gel-filled channels that allowed for molecular sieving of nucleic acids. Pin-electrodes in the chip were used to create electrokinetic forces capable of driving molecules through these micro-channels to perform electrophoretic separations. Ribosomal peaks were measured by fluorescence signal and displayed in an electropherogram. A successful total RNA sample featured 2 distinct ribosomal peaks (18S and 28S rRNA).

### Biotinylated cRNA Hybridization Target.

Total RNA was prepared for use as a hybridization target as described in the manufacturer's instructions for CodeLink Expression Bioarrays(TM) (Amersham Biosciences). The CodeLink Expression Bioarrays utilize nucleic acid

125

hybridization of a biotin-labeled complementary RNA (cRNA) target with DNA oligonucleotide probes attached to a gel matrix.

The biotin-labeled cRNA target is prepared by a linear amplification method. Poly (A) + RNA (within the total RNA population) is primed for reverse transcription by a DNA oligonucleotide containing a T7 RNA polymerase promoter 5' to a (dT) 24 sequence. After second-strand cDNA synthesis, the cDNA serves as the template in an in vitro transcription (IVT) reaction to produce the target cRNA. The IVT is performed in the presence of biotinylated nucleotides to label the target cRNA. This procedure results in a 50-200 fold linear amplification of the input poly (A) + RNA.

#### Hybridization Probes.

The oligonucleotide probes were provided by the Codelink Uniset Mouse I Bioarray (Amersham, product code 300013). Amine-terminated oligonucleotide probes are attached to a three-dimensional polyacrylamide gel matrix. There are 10,000 oligonucleotide probes, each specific to a well-characterized mouse gene. Each mouse gene is representative of a unique gene cluster from the fourth quarter 2001 Genbank Unigene build. There are also 500 control probes.

The sequences of the probes are proprietary to Amersham. However, for each probe, Amersham identifies the corresponding mouse gene by NCBI accession number, OGS, LocusLink, Unigene Cluster ID, and description (name). This information should be available from Amersham. In the case of the differentially expressed probes, this information is duplicated in master table 1. For the complete list, see [http://www4.amershambiosciences.com/apatrix/upp01077.nsf/Content/codelink\\_literature](http://www4.amershambiosciences.com/apatrix/upp01077.nsf/Content/codelink_literature)

Under "Gene Lists", select "Uniset Mouse I", and a gene

list, in Excel format, can be downloaded.

### Hybridization

Using the cRNA target, the hybridization reaction mixture is prepared and loaded into array chambers for bioarray processing as set forth in the manufacturer's instructions for CodeLink Gene Expression Bioarrays™ (Amersham Biosciences). Each sample is hybridized to an individual microarray. Hybridization is at 37°C. The hybridization buffer is prepared as set forth in the Motorola instructions. Hybridization to the microarray is detected with an avidinated fluorescent reagent, Streptavidin-Alexa Fluor® 647 (Amersham).

### Mouse Gene Expression Analysis

Processed arrays were scanned using a GenePix 4000B Microarray Scanner (Axon Instruments, Inc.); array images were acquired using the Amersham CodeLink™ Analysis Software (Release 2.2). The Amersham CodeLink™ Analysis Software gives an integrated optical density (IOD) value for every spot; a unique background value for that spot is subtracted, resulting in "raw" data points. Individual chips are then normalized by the Amersham CodeLink™ software according to the median raw intensity for all 10,000 genes. A negative control threshold (0.2) was also calculated according to the control probes. A significant difference in expression between samples was defined as a minimum of 2-fold change in expression values. Genes with expression values below the negative control threshold were eliminated from the analysis and then the expression data was analyzed to identify genes whose expression levels changed significantly with respect to age.

The list of genes in the tables is a combination of two analyses. Samples of average age 35, 49, 77 and 133 days were compared pair-wise in all possible combinations (6 comparisons) and genes showing differences in expression

greater than 2-fold were listed in the table. (The 56 day data was not included in the comparisons.) The remaining samples were divided into three groups (118 days (2 mice): young; 207 and 403 (4 mice) averaged together: medium; 558 and 725 (4 mice) averaged together: old), the three groups were compared in all possible pair-wise combinations (3 comparisons) and genes showing differences in expression greater than 2-fold were added to the table.

) **Database Searches** Nucleotide sequences and predicted amino acid sequences were compared to public domain databases using the Blast 2.0 program (National Center for Biotechnology Information, National Institutes of Health). Nucleotide sequences were displayed using ABI prism Edit View 1.0.1 (PE Applied Biosystems, Foster City, CA).

Nucleotide database searches were conducted with the

128

never submitted to an archival database but is available in the literature. A small number of sequences are provided through collaboration; the underlying primary sequence data is available in GenBank, but may not be available in any one GenBank record. RefSeq sequences are not submitted primary sequences. RefSeq records are owned by NCBI and therefore can be updated as needed to maintain current annotation or to incorporate additional sequence information." See also <http://www.ncbi.nlm.nih.gov/LocusLink/refseq.html>

It will be appreciated by those in the art that the exact results of a database search will change from day to day, as new sequences are added. Also, if you query with a longer version of the original sequence, the results will change. The results given here were obtained at one time and no guarantee is made that the exact same hits would be obtained in a search on the filing date. However, if an alignment between a particular query sequence and a particular database sequence is discussed, that alignment should not change (if the parameters and sequences remain unchanged).

#### Northern Analysis.

Northern analysis may be used to confirm the results. Favorable and unfavorable genes, identified as described above, or fragments thereof, will be used as probes in Northern hybridization analyses to confirm their differential expression. Total RNA isolated from subject mice will be resolved by agarose gel electrophoresis through a 1% agarose, 1 % formaldehyde denaturing gel, transferred to positively charged nylon membrane, and hybridized to a probe labeled with [32P] dCTP that was generated from the aforementioned gene or fragment using the Random Primed DNA Labeling Kit (Roche, Palo Alto, CA), or to a probe labeled with digoxigenin according to the manufacturer's instructions (Roche, Palo Alto, CA).

### Real-Time RNA Analysis.

Real-time RNA analysis may also be used for confirmation. For "real-time" RNA analysis, RNA will be converted to cDNA and then probed with gene-specific primers made for each clone. "Real-time" incorporation of fluorescent dye will be measured to determine the amount of specific transcript present in each sample. Sample differences (older vs. younger) of 2-fold or greater (in either direction) will be considered differentially expressed. Confirmation using several independent animals is desirable.

### In situ Hybridization

Another form of confirmation may be provided by nonisotopic *in situ* hybridizations (NISH) on selected human (obtained by Tissue Informatics) and mouse tissues using cRNA probes generated from mouse genes found to be up- or down-regulated during aging. *In situ* hybridizations may also be performed on mouse tissues using cRNA probes generated from differentially expressed DNAs. These cRNA's will hybridize to their corresponding messenger RNA's present in cells and will provide information regarding the particular cell types within a tissue that is expressing the particular gene as well as the relative level of gene expression. The cRNA probes may be generated by *in vitro* transcription of template cDNA by Sp6 or T7 RNA polymerase in the presence of digoxigenin-11-UTP (Roche Molecular Biochemicals, Mannheim, Germany; Pardue, M.L. 1985. In: *In situ* hybridization, Nucleic acid hybridization, a practical approach: IRL Press, Oxford, 179-202).

### Transgenic Animals.

Transgenic expression may be used to confirm the results. In one embodiment, a mouse is engineered to overexpress the favorable or unfavorable mouse gene in question. In another embodiment, a mouse is engineered to express the

130

corresponding favorable or unfavorable human gene. In a third embodiment, a nonhuman animal other than a mouse, such as a rat, rabbit, goat, sheep or pig, is engineered to express the favorable or unfavorable mouse or human gene.

### Hyperquantitative Tissue Analysis

In addition to gene expression analysis the tissue sections can also be analyzed using TissueInformatics, Inc's TissueAnalytics™ software. A single representative section may be cut from each tissue block, placed on a slide, and stained with H&E. Digital images of each slide may be acquired using an research microscope and digital camera (Olympus E600 microscope and Sony DKC-ST5). These images were acquired at 20x magnification with a resolution of 0.64 mm/pixel. A hyperquantitative analysis may be performed on the resulting images: First a digital image analysis can identify and annotate structural objects in a tissue using machine vision. These objects, that are constituents of the tissue, can be annotated because they are visually identifiable and have a biological meaning. (By way of example, for liver, the constituents can be, e.g., hepatocytes, sinusoids, vacuoles.) Subsequently a quantification of these structures regarding their geometric properties like area or stain intensities and their relationship to the field of view or per unit area in terms of a % coverage may be performed. Features or parameters for hyper-quantification are specific for each tissue, and may also include relations between features, measures of overall heterogeneity, including orientation, relative locations, and textures.

### Correlation Analysis

Mathematical statistics provides a rich set of additional tools to analyze time resolved data sets of hyper-quantitative and gene expression profiles for similarities, including rank correlation, the calculation of regression



and correlations coefficients, and clustering. Continuous functions may also be fitted through the data points of individual gene and tissue feature data. Relation between gene expression and hyper-quantitative tissue data may be linear or non-linear, in synchronous or asynchronous arrangements.

#### Introduction to Master Tables

The master tables reflect applicants' analysis of the gene chip data.

For each probe corresponding to a differentially expressed mouse gene, Master Table 1 identifies

Col. 1: The mouse gene (upper) and mouse protein (lower) database accession #s.

Col. 2: The corresponding mouse Unigene Cluster, as of the 4<sup>th</sup> Quarter 2001 build.

Col. 3: The behavior (differential expression) observed for the mouse gene. This column identifies the gene as favorable(F) or unfavorable (U) on the basis of its differential behavior in the comparisons (older vs. younger). As more than one older vs. younger comparison is made, only the result of the comparison yielding the greatest differential is listed. In the case of a gene with mixed behavior, both the result of the comparison yielding the greatest favorable differential and the result of the comparison yielding the greatest unfavorable differential are listed. If the value is followed by a parenthetical of the form "(X to Y)", it means that the differential value is the ratio when the absolute value for X weeks was compared to the absolute value for Y weeks, with the ratio being taken as greater-to-lesser.

One possible way of characterizing the degree of differential expression for a particular comparison would be to take the ratio of older to younger. If that ratio is at least 2:1, the behavior is considered unfavorable, and if it is not more than 0.5:1, it is unfavorable.

Use of an older/younger ratio is awkward when one wants to compare the degree of differential expression without regard to the direction of change. Consequently, in the Master Table, the numerical value is the ratio of the greater value to the lesser value. If this ratio is at least two fold, the degree of differential expression is considered significant.

In some of the related applications cited above, and perhaps occasionally in this application, a ratio may be given as a negative number. This does not have its usual mathematical meaning; it is merely a flag that in the comparison, the older value was less than the younger one, i.e., the gene was favorable. For the purpose of applying the teachings of the specification concerning desired ratios, any negative value should be converted to a positive one by taking its absolute value.

Col. 4: A related human protein, identified by its database accession number. Usually, several such proteins are identified relative to each mouse gene. These proteins have been identified by BLAST searches, as explained in cols. 6-8.

Col. 5: The name of the related human protein.

Col. 6: The score (in bits) for the alignment performed by the BLAST program.

Col. 7: The E-value for the alignment performed by the BLAST

program. It is worth noting that Unigene considers a Blastx E Value of less than  $1e-6$  to be a "match" to the reference sequence of a cluster.

- 5 Unless otherwise indicated, the bit score and E-value for the alignment is with respect to the alignment of the mouse DNA of col. 1 to the human protein of col. 4 by BlastX, according to the default parameters.

0

Master Table 1 is divided into two or three subtables on the basis of the Behavior" in col. 3. If a gene has at least one favorable behavior, and no unfavorable ones, it is put into Subtable 1A. In the opposite case, it is put into  
5 Subtable 1B. If any of the genes has mixed behavior, then Master Table 1 will include Subtable 1C for such genes.

Master Table 2 has just three columns.

- 3 Col. 1: Mouse gene.

Col. 2: behavior. Same as col. 3 in Master table 1.

- Col. 3: Human protein classes. Based on the related human  
5 proteins defined in Master Table 1, Master Table 2 generalizes, if possible as to classes of human proteins which are expected to have similar behavior. For a given mouse gene, several human protein classes may be listed because of the diversity of the human proteins found to be  
3 related. In some cases, the stated human protein classes may be hierarchial, e.g., one may be a subset of another. In other cases, the stated classes may be non-overlapping but related. And in yet other cases, the stated classes may be non-overlapping and unrelated. Combinations of the above are  
5 also possible.

134

In addition to the classes stated, the corresponding human gene clusters are also of interest. These may be obtained in a number of ways. First, one may search on Unigene (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=unigene>) for the identified human protein. Review the "hits" (each of which is a Unigene record) for those prefixed by "Hs." Secondly, one may access the Unigene record for the mouse gene cluster (which is given in Master Table 1), and then click on "Homologene". This will bring up a new page which includes the section "Possible Homologous Genes". One of the entries should be a Homo sapiens gene (considered by Unigene to be the most related human gene); click on its Unigene record link.

Additional information of interest may be accessed by searching with the mouse gene accession # in the Mouse Gene Informatics database, at <http://www.informatics.jax.org/>.

The related applications may contain reference to "2-16 week old mice". In the anti-diabetes series of applications, 3 week mice were put on a diet to induce obesity, hyperinsulinemia and diabetes. The 2-16 week old mice were more accurately described as mice who had been on that diet for 2-16 weeks, i.e., they were actually 5-19 weeks (35-133 days) old. Even some of the anti-aging series of applications made reference to 2-16 week old mice, even though the mice were in fact 5-19 weeks (35-133 days) old.

135

Table 1A: Favorable Genes/Proteins

Mouse Gene Protein	Unigene	Behavior	H u m a n Proteins	Description	Bits	E
NM_008334.1	Mm.21300	F:13.28 (5to1)	AAH35263.1	Similar to insulin-like growth factor binding protein 1	384	1E-106
NP_032367.1			CAA68770.1	IGF-binding preprotein (AA_25 to 234)	384	1E-106
			NP_000587.1	Insulin-like growth factor binding protein 1	382	1E-106
			AAA52540.1	Insulin-like growth factor binding protein precursor	338	9E-93
			CAA33110.1	small IGF-binding-protein	192	5E-50
NM_005669	Mm.324	F:8.34 (5to7)	NP_000690.1	amylase, alpha 2A; pancreatic; Amylase, pancreatic, alpha-2A	952	0
NP_033799.1			NP_066188.1	amylase, alpha 2B; pancreatic; Amylase, pancreatic, alpha-2B	946	0
			XP_086988.1	similar to Alpha-amylase, salivary precursor (1,4-alpha-D-glucan glucanohydrolase)	941	0
			67366	alpha-amylase (EC 3.2.1.1) precursor, salivary	939	0
			NP_004029.1	amylase, alpha 1A; salivary; Amylase, salivary, alpha-1A	939	0
			7245760	Chain A, Structure Of Human Pancreatic Alpha-Amylase In Complex With The Carbohydrate Inhibitor Acarbose	927	0
			1421331	Chain, Mol. wt. 1; Molecule: Human Pancreatic Alpha-Amylase; Chain: Null; Ec: 3.2.1.1	925	0
			18655894	Chain A, Three Dimensional Structure Analysis Of The R195q Variant Of Human Pancreatic Alpha Amylase	924	0
			18655893	Chain A, Three Dimensional Structure Analysis Of The R337q Variant Of Human Pancreatic Alpha Amylase	924	0
			14719496	Chain A, Subsite Mapping Of The Active Site Of Human Pancreatic Alpha-Amylase Using Substrates, The Pharmacological Inhibitor Acarbose, And An Active Site Variant	923	0

5

10

15

20

136

20664071				Chain A, Mechanistic Analyses Of Catalysis In Human Pancreatic Alpha-Amylase: Detailed Kinetic And Structural Studies Of Mutants Of Three Conserved Carboxylic Acids	923	0
20664068				Chain A, Three Dimensional Structure Analysis Of The R195a Variant Of Human Pancreatic Alpha Amylase	923	0
13655892				Chain A, Three Dimensional Structure Analysis Of The R337a Variant Of Human Pancreatic Alpha-Amylase	923	0
20664074				Chain A, Mechanistic Analyses Of Catalysis In Human Pancreatic Alpha-Amylase: Detailed Kinetic And Structural Studies Of Mutants Of Three Conserved Carboxylic Acids	922	0
1633119				Chain, Human Salivary Amylase	919	0
15988375				Chain A, Role Of Mobile Loop In The Mechanism Of Human Salivary Amylase	914	0
15988376				Chain A, Role Of Ethic Mobile Loop In The Mechanism Of Human Salivary Amylase	904	0
AAA57345.1				alpha-amyase	515	1E-146
NP_005710.1				actin related protein 2/3 complex subunit 3; ARP2/3 protein complex subunit p21	365	1E-101
NP_062798.1				p21-Arc	363	1E-100
NP_062798.1				p21-Arc	363	1E-100
CAC14083.1				d470L14.3 (novel protein similar to the Arp2/3 protein complex subunit p21-Arc (ARC21))	350	8E-97
XP_167194.1				similar to ARP2/3 complex 21 kDa subunit (P21-ARC) (Actin-related protein 2/3 complex subunit 3)	215	4E-56
NP_062798.1				Lipin 1	1493	0
NP_062798.1				Lipin 1	1488	0
NP_062798.1				Similar to lipin 1	1487	0
NP_062798.1				similar to Hypothetical protein KIAA0188	1476	0

5

10

15

20

137

				NP_053461.1	lipin 2			790	0
NM_009117	Mm.148800	F:4.72 (5to19)		NP_000322.1	serum amyloid A1			169	3E-43
NP_033143.1									
NM_015805	Mm.104687	F:4.48 (5to7)		O75110	Potential phospholipid-transporting ATPase IIA			1539	0
NP_056620.1				XP_030577.3	similar to Potential phospholipid-transporting ATPase IIA			1327	0
				BAA31586.1	KJAA0611 protein			1178	0
				CAB63450.1	dj1114A1.1 (ATPase, class II, type 9A (KJAA0611))			1133	0
				XP_085762.3	similar to ATPase, class 2, member b; ATPase 9B, class II; ATPase 9B, p type			658	0
				O43861	Potential phospholipid-transporting ATPase IIB (HUSSY-20)			615	1E-175
				AAO0243.1	putative ATPase			610	1E-174
				CAA06934.1	ATPase			609	1E-174
NM_007706	Mm.4132	F:4.4 (YtoM)		NP_003868.1	suppressor of cytokine signaling-2; STAT induced STAT inhibitor-2; cytokine-inducible SH2 protein 2			364	1E-100
NP_031732.1				JC5626	STAT induced STAT inhibitor 2			361	1E-100
				JC5760	cytokine-inducible SH2 protein 2			360	3E-99
				BAA22536.1	CIS2			359	3E-99
				AAO98896.1	suppressor of cytokine signalling-2; HSSOCS-2			350	3E-96
NM_008640	Mm.30071	F:4.09 (5to19)		NP_055528.1	lysosomal-associated protein transmembrane 4 alpha; membrane nucleoside transporter;			390	1E-108
NP_032666.1					lysosomal-associated protein transmembrane 4				

25

30

35

40

138

				AAH03158.1	lysosomal-associated protein transmembrane 4 alpha	339	1E-107
A K 0 0 4 8 5 1	Mm.21679	F:4.06 (5to19)		NP_061821.1	Gene 33/Mig-6	641	0
NP_598514.1				AA835056.1	[Mig-6=mitogen-inducible gene mig-6 product [human, WI-38 cells, Peptide, 462 aa]	635	1E-180
				T46346	hypothetical protein DKFZp434I114.1	291	4E-77
M 6 3 2 4 5	Mm.19143	F:3.98 (5to19)		NP_000679.1	aminolevulinate, delta-, synthase 1	833	0
AA491867.1				CAA68506.1	5-aminolevulinate synthase precursor	808	0
				CAB06076.1	5-aminolevulinic acid synthase	645	0
				P22557	5-aminolevulinic acid synthase, erythroid-specific, mitochondrial precursor (Delta-aminolevulinate synthase) (Delta-ALA synthetase) (ALAS-E)	645	0
				CAA39795.1	delta-aminolevulinate synthase (erythroid)	644	0
				NP_000023.1	aminolevulinate, delta-, synthase 2; Aminolevulinate, delta-, synthase-2	644	0
				AAH0230.1	Similar to aminolevulinate, delta-, synthase 2 (sideroblastic/hypochromic anemia)	642	0
A K 0 0 5 2 7 4	Mm.195961	F:3.89 (5to7)		NP_115680.1	hypothetical protein MGC2405	471	1E-131
BA823924.1				AAK61250.1	similar to HAGH	376	1E-103
				NP_095317.1	hydroxyacyl glutathione hydrolase; hydroxyacyl glutathione hydrolase; glyoxalase 2;	266	6E-70
					Hydroxyacyl glutathione hydrolase; glyoxalase II; hydroxyacylglutathione hydroxylase		
				BA870814.1	unannotated protein product	237	2E-69

5

10

15

20



139

NM_026346	Mm.40466	F:3.64 (YtoO)	NP_478136	F-box only protein 32 isoform 1; muscle atrophy F-box protein; atrogin-1	710	0
NP_080622.1						
			BA885128	F-box domain Fbx25-containing protein	446	1E-123
			NP_680482	F-box only protein 32 isoform 2; muscle atrophy F-box protein; atrogin-1	422	1E-116
			AAH324030	similar to RIKEN cDNA 4833442G10 gene (H. sapiens)	417	1E-115
			AAF04526	F-box protein Fbx25	354	3E-96
			NP_036305	F-box only protein 25; F-box protein Fbx25	353	6E-96
NM_025298	Mm.30605	F:3.45 (YtoM)	NP_060589	RNA polymerase III 80 kDa subunit RPC5	1288	0
NP_079574.1						
			AAAM18215	RNA polymerase III 80 kDa subunit RPC5	1286	0
			BAB14481	unnamed protein product	1218	0
			AAH00285	hypothetical protein FLJ10509	1191	0
			BAB14437	unnamed protein product	1187	0
			BAA95976	KIAA1452 protein	1121	0
NM_022331	Mm.29151	F:3.44 (5to19)	NP_055500.1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1; MMS-inducible gene	592	1E-168
NP_071726.1			AAC09357.1	unknown	525	1E-147
			AAAG17233.1	unknown	295	2E-78
			AAH09739.1	Similar to homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	218	2E-55
			NP_071768.2	hypothetical protein FLJ22313	216	1E-54
NM_016773	Mm.9901	F:3.41 (YtoO)	NP_005004.1	nucleobindin 2	675	0
NP_058053.1			AAAM73810.1	NUCB2 protein	669	0

5

10

15

20

25

140

			NP_006175.2	nucleobindin 1		424	1E-118
			Q02818	Nucleobindin 1 precursor (CALNOC)		418	1E-116
			AAA36383.1	nucleobindin		414	1E-115
			BAC11593.1	unnamed protein product		384	1E-105
			NP_110382.1	thioredoxin-related transmembrane protein		383	1E-105
			T12471	hypothetical protein DKFZp564E1962.1		383	1E-105
			AAH36460.1	Similar to thioredoxin domain-containing		381	1E-104
			AAH33787.1	hypothetical protein DJ971N18.2		202	1E-50
			BAC11237.1	unnamed protein product		202	1E-50
			CAC17521.1	dJ971N18.2.1 (novel protein (isoform 1))		202	1E-50
			NP_002301.1	leukemia inhibitory factor receptor precursor		1663	0
			AAAB23884.1	leukaemia inhibitory factor receptor, LIF receptor [human, placenta, Peptide, 1078 aa]		1640	0
			NP_003990.1	oncostatin M receptor		345	2E-94
			AAAB1897.1	leukemia inhibitory factor receptor		282	2E-75
			NP_000230.1	lysozyme precursor		233	6E-62
			AAAB36188.1	lysozyme precursor (EC 3.2.1.17)		233	2E-61
			AAC63078.1	lysozyme precursor		228	2E-60

5

10

15

20

141

				Chain A, Crystal Structure Of Mutant Human Lysozyme With Four Extra Residues (Erea) At The N-Terminal	Chain A, Verification Of Sprp Using Mutant Human Lysozymes	228	2E-60
						228	3E-60
A K 0 5 4 6	Mm.33326	F:3.33 (5to19)	NP_000119.1	plasma coagulation factor XI precursor, isoform 4; plasma thromboplastin antecedent		1048	0
BAB24114.1			AAA51985.1	coagulation factor XI		1044	0
			NP_062505.1	platelet coagulation factor XI, isoform b; plasma thromboplastin antecedent		848	0
			NP_000883.1	plasma kallikrein B1 precursor; Kallikrein, plasma; kallikrein 3, plasma; kallikrein B plasma, Fletcher factor		755	0
			AACS1784.1	serine protease		217	5E-55
			AAK53559.1	epitheliasin		216	1E-54
			AAK29280.1	androgen-regulated serine protease TMPRSS2, precursor		216	1E-54
			NP_005647.2	transmembrane protease, serine 2; epitheliasin		216	1E-54
NM_010286	Mm.22216	F:3.32 (5to19)	Q99576	Glucocorticoid-induced leucine zipper protein (Delta sleep-inducing peptide immunoreactor)		196	8E-49
NP_034416.1				(DSIP-immunoreactive peptide) (DIP protein) (hDIP) (TSC-22-like protein) (TSC-22R)			
			T14749	Hypothetical protein DKFP266A093.1		188	2E-46
NM_009344	Mm.3117	F:3.29 (7to19)	NM_009344	pleckstrin homology-like domain, family A, member 1; PQ-rich protein		379	1E-104
NP_033370.1			NP_033370.1				
			AAH18929.1	Similar to T-cell death associated gene		235	1E-60

5

10

15

20

## 1.4.2

A.K.0.0.5.3.5	Mm.29483	IF:3.25 (YcoM)	NP_570901.1	solute carrier family 39 (zinc transporter), member 4	700	0
BAB24106.1			NP_060237.1	solute carrier family 39 (zinc transporter), member 4	578	1E-172
NM_003994.1	Mm.35605	IF:3.24 (YcoO)	CAA79356.1	E-cadherin	1253	0
			NP_004351.1	cadherin 1, type 1 preproprotein; calcium-dependent adhesion protein, epithelial; cadherin 1, E-cadherin (epithelial); uvomorulin; cell-CAM 120/80; Ate-1	1249	0
			BAA88957.1	E-cadherin	1238	0
			CAA84586.1	E-cadherin	1179	0
			AAA61259.1	uvomorulin	1151	0
			BAA88956.1	E-cadherin	981	0
			P22223	Cadherin-3 precursor (Placental-cadherin) (P-cadherin)	749	0
			NP_001784.2	cadherin 3, type 1 preproprotein; P-cadherin; placental cadherin; cadherin 3, P-cadherin (placental); calcium-dependent adhesion protein, placental	746	0
			P19022	Neural-cadherin precursor (N-cadherin) (Cadherin-2)	381	1E-165
			NP_001783.2	cadherin 2, type 1 preproprotein; N-cadherin 1; cadherin 2, N-cadherin (neuronal); neural cadherin; calcium-dependent adhesion protein, neuronal	381	1E-165
			AAB22854.1	N-cadherin	381	1E-163
			IJHUCN	cadherin 2 precursor	579	1E-164
			AAH36470.1	cadherin 2, type 1, N-cadherin (neuronal)	574	1E-163
			NP_001785.2	cadherin 4, type 1 preproprotein; cadherin 4, R-cadherin (retinal); R-cadherin; retinal cadherin	556	1E-158
			P55283	Cadherin-4 precursor (Retinal-cadherin) (R-cadherin) (R-CAD)	540	1E-153
			AAA03236.1	N-cadherin	539	1E-152

143

			CAA40773.1	N-cadherin		526	1E-148
			BAC03677.1	unnamed protein product		523	1E-147
NM_007687	Mm.4024	F:3.24 (Sto7)	NP_005498.1	cofilin 1 (non-muscle)		327	1E-88
NP_031713.1			NP_068733.1	cofilin 2 isoform 1		274	1E-72
			XP_171270.1	similar to COFILIN, NON-MUSCLE ISOFORM		261	1E-68
			XP_060203.1	similar to Cofilin, non-muscle isoform (18 kDa phosphoprotein)(P18)		248	8E-65
			NP_006861.1	desmin (actin depolymerizing factor); desmin		237	3E-61
AK005989	Mm.18259	F:3.2 (YtoM)	NP_005733.1	protein disulfide isomerase-related protein		714	0
BA324354.1			AAB50217.1	protein disulfide isomerase-related protein 5		681	0
NM_008904	Mm.10707	F:3.2 (YtoM)	AAD51615	PPAR gamma coactivator-1		1273	0
NP_032970.1			NP_037393	peroxisome proliferative activated receptor, gamma, coactivator 1		1272	0
NM_026508	Mm.182051	F:3.15 (YtoM)	NP_057376.1	tumor necrosis factor type 1 receptor associated protein		1214	0
NP_080784.1							
			AAH18950.1	Unknown (protein for MGC15157)		1214	0
			AAH01455.1	heat shock protein 75		1208	0
			AA00679.1	heat shock protein 75		1144	0

5

10

15

20

144

			A55877	tumor necrosis factor type 1 receptor associated protein TRAP-1	1108	0
			AAC24722.1	TRAP1	1082	0
			BAC04136.1	unnamed protein product	990	0
			AAH02994.1	Unknown (protein for MGC:3823)	741	0
			AAK74072.1	heat shock protein gp96 precursor	324	3E-88
			NP_003290.1	tumor rejection antigen (gp96) 1; Tumor rejection antigen-1 (gp96)	323	7E-88
			NP_062558.1	hypothetical protein R30953_1	229	2E-39
NM_021792	Mm.29008	F:3.14 (5to19)				
NP_068564.1						
NM_025404	Mm.3376	F:3.11 (5to11)	AAH00043.1	ADP-ribosylation factor 4-like	359	6E-98
NP_079680.1			NP_001652.1	ADP-ribosylation factor 4-like; ADP-ribosylation factor-like 6	357	2E-97
			AAJ93229.1	ADP-ribosylation factor	348	1E-94
			XP_045890.2	similar to ADP-ribosylation factor 4L	233	4E-60
			NP_005729.1	ADP-ribosylation factor-like 4	209	9E-57
			NP_005728.2	ADP-ribosylation factor-like 7	148	1E-52
AK_005035	Mm.18802	F:3.09 (5to19)	NP_001054.1	transferrin	853	0
BA023762.1			pdbj LFG	Lactoferrin (Diferric)	797	0
			pdbj LFH	Lactoferrin (Apo Form)	797	0
			pdbj LFI	Lactoferrin (Copper Form)	797	0
			pdbj FCG	Lactoferrin	797	0

5

10

15

20

145

	AAA59479.1	neutrophil lactoferrin		796	0
	pdj1B0L	Lactoferrin		796	0
	pdj1CB6	Lactoferrin		796	0
	CAA37116.1	precursor lactoferrin (709 AA)		796	0
	P02788	Lactotransferrin precursor (Lactoferrin) [Contains: Lactoferrin A; Lactoferrin B; Lactoferrin C]		796	0
	pdj1LCF	Lactoferrin (Copper and Oxalate Form)		796	0
	AAH15822.1	lactotransferrin		796	0
	AAA36139.1	lactoferrin		795	0
	AAA58656.1	III F2		795	0
	AAH22347.1	lactotransferrin		795	0
	AA648753.1	lactoferrin precursor		794	0
	AAA59511.1	lactoferrin		793	0
	AAH15823.1	lactotransferrin		793	0
	NP_002334.1	lactotransferrin		792	0
	AAF22007.1	PRO1400		709	0
	AAA61141.1	transferrin		622	1E-177
	AAB57795.1	Lactoferrin. Incomplete at NH2 end		570	1E-161

5

10

15

146

			XP_067170.1	similar to RIKEN cDNA 1300017.02	550	1E-155
			pdh1JQF	Serotransferrin	443	1E-123
			pdh1BP5	Serum Transferrin	443	1E-123
			pdh1FOE	Serotransferrin	441	1E-122
			pdh1A8E	Serum Transferrin	440	1E-122
			pdh1JQF	Transferrin	440	1E-122
			pdh1D3K	Serum Transferrin	439	1E-121
			pdh1DTG	Transferrin	438	1E-121
			pdh1B3E	Serum Transferrin	437	1E-121
			pdh1D4N	Transferrin	437	1E-121
			NP_005920.1	melanoma-associated antigen p97, isoform 1, precursor; melanotransferrin; melanoma-associated antigen p97	394	1E-108
			pdh1LCT	Lactoferrin (N-Terminal Half-Molecule)	372	1E-101
			pdh1EH3	Lactoferrin	372	1E-101
			pdh1L5T	Lactoferrin	370	1E-101
			pdh1VFE	Human Lactoferrin	370	1E-101
			pdh1DSN	Lactoferrin	368	1E-100
			pdh1VFD	Lactoferrin	367	1E-100
			CAC14276.1	ba11216.1 (CCAAT/enhancer binding protein (C/EBP), beta)	271	2E-72
			NP_005185.1	CCAAT/enhancer binding protein (C/EBP), beta; CCAAT/enhancer-binding protein (C/EBP), beta (transcription factor-5)	271	2E-72
			AAH44572	similar to solute carrier family 15 (H+/peptide transporter), member 2	1128	0
			NP_066568	solute carrier family 15 (H+/peptide transporter), member 2	1122	0
			AAC15477	Caco-2 oligopeptide transporter	561	1E-159

5

10

15

20

25



NP_005064					solute carrier family 15 (oligopeptide transporter), member 1; Human peptide transporter (HPEPT1) mRNA, complete cds	561	1E-159
CAC27442					BA551M18.1.1 (solute carrier family 15 (oligopeptide transporter) member 1)	502	1E-141
JC5638					pH-sensing regulatory factor	231	5E-60
NP_003716					3-hydroxysteroid epimerase; oxidative 3-alpha-hydroxysteroid-dehydrogenase; 3(alpha->beta)-hydroxysteroid epimerase; retinol dehydrogenase; oxidoreductase; NAD+-dependent 3 alpha-hydroxysteroid dehydrogenase	473	1E-133
AA188252					oxidative 3 alpha hydroxysteroid dehydrogenase	442	1E-124
AAC39922					sterol/retinol dehydrogenase	404	1E-112
NP_003699					microsomal NAD+-dependent retinol dehydrogenase 4	399	1E-111
NP_683695					orphan short-chain dehydrogenase / reductase; retinol dehydrogenase similar protein	312	7E-85
NP_005762					NAD(P) dependent retinol dehydrogenase/reductase; 3-alpha hydroxysteroid dehydrogenase	300	3E-81
Q92781					11-cis retinol dehydrogenase (11-cis RDH)	283	4E-76
AAH28298					Similar to retinol dehydrogenase 5 (11-cis and 9-cis)	281	1E-75
NP_002896					retinol dehydrogenase 5 (11-cis and 9-cis); retinol dehydrogenase 5 (11-cis and 9-cis)	272	1E-72
AAD32458					retinol dehydrogenase homolog	267	2E-71
AAH82748					retinol dehydrogenase homolog isoform-1	252	1E-66
NP_055400.1					solute carrier family 11 (proton-coupled divalent metal ion transporters), member 3; ferroportin 1; iron regulated gene 1; ferroportin 1	936	0
NP_058613.1					SLC11A3 iron transporter	933	0
AAH35893.1					solute carrier family 11 (proton-coupled divalent metal ion transporters), member 3	932	0
BA092049.1					unnamed protein product	302	2E-81
NP_000763.1					cytochrome P450, subfamily 11C (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily 11C (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase	629	1E-179
NP_034134.1					Cytochrome P450 2C18 (CYP2C18) (P450-6B/29C)	627	1E-178

148

NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	618	1E-176
E38462	S-mephenytoin 4'-hydroxylase (EC 1.1.1.4.-) cytochrome P450 2C19	612	1E-174
AAB23864.2	cytochrome P-450	611	1E-174
BAA00123.1	cytochrome P-450	611	1E-174
I506290A	cytochrome P450	610	1E-173
P11712	Cytochrome P450 2C9 (CYP11C9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP).	611	1E-174
AAA52157.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	605	1E-172
P10632	Cytochrome P450 2C8 (CYP11C8) (P450 form 1) (P450 MP-12/MP-20) (P450 IIC2) (S-mephenytoin 4-hydroxylase)	600	1E-170
AAH20596.1	Unknown (protein for MGC-27146)	599	1E-170
AAA52161.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	598	1E-170
AAB35292.1	cytochrome P450 arachidonic acid epoxidase isoform, Cyp 2C8 [human, kidney, Peptide Partial, 485 aa]	596	1E-169
AAA36660.1	cytochrome P450	598	1E-170
AAA35739	cytochrome P-450 1	597	1E-169
AAB35292.1	cytochrome P450 arachidonic acid epoxidase isoform, Cyp 2C8 [human, kidney, Peptide Partial, 485 aa]	596	1E-169
AAA52160	cytochrome P-450 S-mephenytoin 4-hydroxylase.	595	1E-169
AAA52145.1	locus HUMCYP2C17	516	1E-145
AAA52159.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	514	1E-144
CAA46778.1	cytochrome P-450 II C	497	1E-139

5

10

15

149

			A31949	cytochrome P450 2E1	478 IE-133
			AA013753.1	cytochrome P450 2E1	478 IE-133
			AA013601.1	cytochrome P450-2E1	478 IE-133
AB060274	Mm.196225	F:3.04 (Ytom)	NP_001944	endothelial cell growth factor 1 (platelet-derived); thymidine phosphorylase; gliostatin	730 0
BAB41208.1					
			AAH18160	endothelial cell growth factor 1 (platelet-derived)	728 0
			P19971	Thymidine phosphorylase precursor (TdkPase) (TP) (Platelet-derived endothelial cell growth factor) (PD-ECGF) (Gliostatin)	728 0
			NP_005129	cytochrome oxidase deficient homolog 2	234 3E-61
			NP_004580	cytochrome oxidase deficient homolog 1	234 3E-61
NM_018887	Mm.17991	F:3 (7to19)	NP_057677.1	oxysterol 7alpha-hydroxylase	712 0
NP_061375.1			AAH10358.1	oxysterol 7alpha-hydroxylase	710 0
NM_024406	Mm.582	F:2.98 (7to19)	NP_001433.1	fatty acid binding protein 4, adipocyte; A-FABP	245 4E-65
NP_077717.1					
NM_018746	Mm.34819	F:2.96 (Ytom)	BAA07536.1	PK-120 precursor	1130 0
NP_061216.1					
			AA005198.1	inter-alpha-trypsin inhibitor family heavy chain-related protein	1127 0
			Q14624	Inter-alpha-trypsin inhibitor heavy chain H4 precursor (IT heavy chain H4) [inter-alpha-inhibitor heavy chain-4] (Inter-alpha-trypsin inhibitor family heavy chain-related protein) (IHRP) (Plasma kallikrein sensitive glycoprotein 120) (PK-120) (GP120) (PRO1851) [Contains: GP57]	1127 0
			NP_002209.1	inter-alpha (globulin) inhibitor H4 (plasma kallikrein-sensitive glycoprotein); inter-alpha (globulin) inhibitor, H polypeptide-like 1; Inter-alpha (globulin) inhibitor, H4 polypeptide	1126 0
			AA069610.1	PRO1851	722 0

5

10

15

20

	S30350				inter-alpha-trypsin inhibitor heavy chain 3 precursor	620 IE-177
	NP_002208.1				pre-alpha (globulin) inhibitor, H3 polypeptide; inter-alpha (globulin) inhibitor, H3 polypeptide	620 IE-177
	P19827				Inter-alpha-trypsin inhibitor heavy chain H1 precursor (ITI heavy chain H1) (inter-alpha-inhibitor heavy chain 1) (inter-alpha-trypsin inhibitor complex component III) (Serum-derived hyaluronan-associated protein) (SHAP)	461 IE-129
	S24391				inter-alpha-trypsin inhibitor heavy chain H1 precursor	461 IE-129
	NP_002206.1				inter-alpha (globulin) inhibitor, H1 polypeptide	461 IE-129
	P19823				Inter-alpha-trypsin inhibitor heavy chain H2 precursor (ITI heavy chain H2) (inter-alpha-inhibitor heavy chain 2) (inter-alpha-trypsin inhibitor complex component II) (Serum-derived hyaluronan-associated protein) (SHAP)	449 IE-125
	NP_002207.1				Inter-alpha (globulin) inhibitor, H2 polypeptide	447 IE-125
	S04484				inter-alpha-trypsin inhibitor chain 3 - human	441 IE-123
	CAA34346.1				inter-alpha-trypsin inhibitor C-terminal	434 IE-121
NM_009744	Mm.13811	F:2.93 (5to19)			B-cell lymphoma 6 protein; B-cell CLL/lymphoma-6; cys-lis2 zinc finger transcription factor BCL5; zinc finger protein 51; lymphoma-associated zinc finger gene on chromosome 3	0
NP_033874.1	A48752				B-cell CLL/lymphoma 6 (BCL6) protein	0
	BAC00962.1				/BAZF	335 IE-91
	XP_171849.1				similar to BcL6-associated zinc finger protein	300 7E-81
NM_017372	Mm.45436	F:2.91 (7to19)			lysosome precursor	
NP_059083.1	AAX36188.1				lysosome precursor (EC 3.2.1.17)	231 3E-61
pdbj C7P					Chain A, Crystal Structure Of Mutant Human Lysozyme With Four Extra Residues (Gaia) At The	228 3E-60

151

					N-Terminal			
					Chain A, Verification Of Spnp Using Mutant Human Lysozymes		227	61-60
					Chain, Lysozyme (E.C.3.2.1.17) Mutant With Arg 115 Replaced By His (R115h)		227	61-60
					Lysozyme precursor		226	115-59
					RING finger protein 25		702	0
					Ring finger protein 25		684	0
					Similar to chitinase 3-like 1 (cartilage glycoprotein-39)		537	1E-152
					chitinase 3-like 1; cartilage glycoprotein-39		536	1E-152
					similar to chitinase 3-like 1 (cartilage glycoprotein-39)		535	1E-152
					chitinotriase; plasma methylumbelliferyl tetra-N-acetylchitinotriase hydrolase		355	8E-98
					chitinotriase precursor		355	1E-97
					Chain A, Crystal Structure Of Human Chitinotriase In Complex With Chitinobiose		345	8E-95
					chitinase 3-like 2; chondrocyte protein 39		340	3E-93
					Chitinase 3-like protein 2 precursor (YKL-39) (Chondrocyte protein 39)		340	3E-93
					chitinase 3-like 2		340	3E-93
					chitinase		340	3E-93
					acidic mammalian chitinase precursor		319	8E-87
					oviductin		274	2E-73
					oviductal glycoprotein		273	5E-73
					oviductal glycoprotein 1, 120kDa (mucin 9, oviductin); mucin 9 (oviductin); oviductal glycoprotein 1, 120kDa (mucin 9, oviductin)		273	5E-73
					oviductal glycoprotein		273	5E-73
					eosinophil chemotactic cytokine		226	9E-59
					Kruppel-like factor 15; KLF protein; kidney-enriched Kruppel-like factor		024	1E-178

45

50

55

09

59

70

152

NM_010634	Mm.741	F:2.84 (5to19)	NP_001435.1	fatty acid binding protein 5 (psoriasis-associated); E-FABP	220	2E-56
NP_034764.1						
NM_009263	Mm.321	F:2.82 (5to19)	BAC11635.1	unnamed protein product	305	2E-82
NP_033289.1						
			P10451	Osteopontin precursor (Bone sialoprotein 1) (Urinary stone protein) (Secreted phosphoprotein 1) (SPP-1) (Nephropontin) (Uropontin)	302	8E-82
			I56986	OPN-a - human (fragment)	298	2E-80
			NP_000573.1	secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1);	276	8E-74
				Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)		
			I76601	OPN-b - human (fragment)	270	4E-72
			I76602	OPN-c - human (fragment)	248	2E-65
NM_007779	Mm.22574	F:2.8 (5to19)	NP_05202.1	colony stimulating factor 1 receptor, formerly McDonough feline sarcoma viral (v-fms) oncogene homolog; C-FMS; Colony-stimulating factor-1 receptor; oncogene FMS (McDonough feline sarcoma)	1392	0
NP_031805.1			P07333	Macrophage colony stimulating factor 1 receptor precursor (CSF-1-R) (Fms proto-oncogene) (c-fms) (CD115 antigen)	1392	0
			NP_000213.1	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog precursor	637	0
			AAC50969.1	KIT protein	634	1E-180
			NP_006197.1	platelet-derived growth factor receptor alpha precursor	479	1E-134
			NP_002600.1	platelet-derived growth factor receptor beta precursor; beta platelet-derived growth factor receptor	473	1E-132
			AAH32224.1	platelet-derived growth factor receptor, beta polypeptide	473	1E-132
			AAA36427.1	platelet-derived growth factor receptor	473	1E-132

5

10

15

20

153

				CAA81393.1	FLT3 receptor tyrosine kinase		419	1E-115
				NP_004110.1	fms-related tyrosine kinase 3		416	1E-114
				A36873	protein-tyrosine kinase (BC 2.7.1.112) STK-1 precursor		408	1E-112
5								
				NP_071914.1	hypothetical protein FLJ21195 similar to protein related to DAC		308	5E-83
				NP_037504.1	cysteine knot superfamily 1, BMP antagonist 1; gremlin		184	1E-45
				AAF64142	NPD008 protein		394	1E-109
10								
				AAH08430	Unknown (protein for MGC:4598)		391	1E-108
				NP_057162	CGI-148 protein		349	7E-96
				NP_660344	similar to CGI-148 protein		293	5E-79
15				NP_001395.1	eukaryotic translation elongation factor 1 gamma; elongation factor 1-gamma; EF-1-gamma; eEF-1B gamma; translation elongation factor eEF-1 gamma chain; PRO1608; pancreatic tumor-related protein		792	0
				AAH13918.1	Similar to eukaryotic translation elongation factor 1 gamma		791	0
				XP_088122.2	similar to Elongation factor 1-gamma (EF-1-gamma) (eEF-1B gamma)		779	0
				AA018414.1	pancreatic tumor-related protein		662	0
20				AAF69604.1	PRO1608		580	1E-165
				NP_057678.1	PK506 binding protein precursor; FK506 binding protein 11 (19 kDa)		294	1E-79
				NP_077131.2				
25				NP_008061	glucose-6-phosphatase, catalytic		588	1E-168

154

NP_032087.1				AAH20700.1	Unknown (protein for MGC:22459)		416	1E-115
				NP_066999.1	islet-specific glucose-6-phosphatase catalytic subunit-related p		318	2E-86
NM_019806	Mm.38800	F:2.74 (Sto19)		NP_004729.1	VAMP (vesicle-associated membrane protein)-associated protein B and C; VAMP-associated protein C; VAMP-associated protein B; VAMP-associated 33 kDa protein		404	1E-113
NP_062780.1				AAF67013.1	VAMP-associated 33 kDa protein		399	1E-111
				AAF72105.1	33 kDa Vamp-associated protein		291	5E-79
				NP_003555.2	vesicle-associated membrane protein (VAMP)-associated protein of 33 kDa; vesicle-associated membrane protein (VAMP), 33 kDa; VAMP-associated protein A; VAMP (vesicle-associated membrane protein)-associated protein A (33kD)		291	8E-79
				AAC26508.1	VAMP-associated protein of 33 kDa		289	3E-78
NM_022324	Mm.30222	F:2.74 (Sto19)		AAH10880.1	Unknown (protein for MGC:1757)		342	5E-94
NP_071719.1				AAH06248.1	stromal cell-derived factor 2-like 1		340	3E-93
				NP_071327.1	stromal cell-derived factor 2-like 1		334	1E-91
				NP_008854.2	stromal cell-derived factor 2 precursor		236	3E-62
				Q99470	Stromal cell-derived factor 2 precursor (SDF-2)		233	5E-61
M_12571	Mm.196559	F:2.73 (Yok4)		NP_005336.2	heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein, dnaK-		635	0
AAA57234.1				P08107	Type molecular chaperone HSP70-1			
					Heat shock 70 kDa protein 1 (HSP70-1) (HSP70-1/HSP70-2)		635	0

5

10

15

20



155

			NP_005337.1	heat shock 70kDa protein 1B; heat shock 70kD protein 1B	633	1E-180
			A29160	dnaK-type molecular chaperone HSP11L	628	1E-179
			XP_175177.1	heat shock 70kD protein 1-like	588	1E-167
			BAA32521.1	Heat shock protein 70 testis variant	586	1E-166
			NP_005518.1	heat shock 70kDa protein 1-like; Heat-shock 70kD protein-like-1; heat shock 70kD protein-like 1; heat shock 70kD protein 1-like	586	1E-166
			XP_166348.1	similar to Heat shock 70 kDa protein 1-HOM (HSP70-HOM)	586	1E-166
			AAH34483.1	heat shock 70kD protein 1-like	585	1E-166
			NP_068814.2	heat shock 70kDa protein 2; heat shock 70kD protein 2; Heat-shock 70kD protein-2	567	1E-160
			AAH36107.1	Unknown (protein for MGC:33922)	567	1E-160
			NP_006588.1	heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kD protein 10; heat shock cognate protein 54; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1	565	1E-160
			AAH07276.1	Similar to heat shock cognate 71-kd protein		
			AAD11466.1	heat shock protein	565	1E-160
			AAH35665.1	heat shock 70kDa protein 6 (HSP70B')	564	1E-159
			NP_002146.1	heat shock 70kDa protein 6 (HSP70B); heat shock 70kD protein 6 (HSP70B'); Heat-shock 70kD protein-6 (HSP70B')	555	1E-157
					552	1E-156
U 8 9 4 1 5	NULL	F:2.73 (5to19)	NP_001952.1	eukaryotic translation elongation factor 2; polypeptidyl-IRNA	444	1E-125
AAC36522.1			XP_170567.1	similar to Elongation factor 2 (EF-2)	438	1E-123
NM_009242	Mm.35439	F:2.73 (5to19)	NP_003109.1	secreted, protein, acidic, cysteine-rich (osteonection); Osteonectin (secreted protein, acidic,	575	1E-163

5

10

15

20

156

NP_033268.1				cysteine-rich)			
		AAA0993.1		osteonectin		573	1E-163
		pdb BMO		SPARC precursor (Secreted protein acidic and rich in cysteine) (Osteonectin) (ON) (Basement membrane protein BM-40)		496	1E-140
		pdb INUB		SPARC precursor (Secreted protein acidic and rich in cysteine) (Osteonectin) (ON) (Basement membrane protein BM-40)		474	1E-133
		AAH33721.1		Unknown (protein for MOC45264)		320	5E-87
		NP_004675.2		SPARC-like 1; mast9; hevvin		320	5E-87
		Q14515		SPARC-like protein 1 precursor (High endothelial venule protein) (Hevin) (MAST 9)		320	5E-87
		pdb ISRA		Chain , Extracellular Matrix Protein Mol_id: 1; Molecule: Sparc; Chair: Null; Fragment: Carboxy-Terminal Domain (Residues 136 - 286); Synonym: Bm-40, Osteonectin; Engineered: Yes; Heterogen: 2 Ca 2+ Ions, One Unidentified Metal Ion Modeled As Ca 2+; Other_details: Crystallized From 0.7 M K <sub>2</sub> Na-Tartrate, Ph 7.5 + 2 Mm Cact2		311	2E-84
NM_026104	Mm.148837	F.2.72 (5cr7)		similar to RIKEN cDNA 1700095F04		305	1E-82
NP_080380.1				unnamed protein product		229	4E-60
A F 2 9 4 6 1 7	Mm.19669	F.2.69 (5cr7)		6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3		1030	0
AA02118.1							
				6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase		1028	0
				6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46)		1028	0
				inducible 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase		1005	0

5

10

15

157

				CAA06605.1	6-phosphofructo-2-kinase		699	0
				O60825	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2 (6PF-2-K/Fru-2,6-P2ASE heart-type isozyme) (PFK-2/FBPase-2) [Includes: 6-phosphofructo-2-kinase; Fructose-2,6-bisphosphatase]		697	0
				NP_006203.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2; Fructose-2,6-bisphosphatase, cardiac isozyme		688	0
				BA019681.1	6-phosphofructo-2-kinase heart isoform		680	0
				NP_004538.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4		670	0
				JC5871	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46)		669	0
				NP_002616.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 1; Fructose-2,6-bisphosphatase		668	0
				P16118	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 1 (6PF-2-K/Fru-2,6-P2ASE liver isozyme) [Includes: 6-phosphofructo-2-kinase; Fructose-2,6-bisphosphatase]		668	0
				CA0306077.1	6-phosphofructo-2-kinase		589	1E-167
NM_007952	Mm.709	F.2.65 (5to19)		AAH36000.1	Unknown (protein for IMAGE:4712175)		888	0
NP_031978.1				NP_005304.3	glucose regulated protein, 58kDa; glucose regulated protein, 58KD		882	0
				JC5704	protein disulfide-isomerase (EC 5.3.4.1) ER60 precursor		882	0
				AAC51518.1	ER-60 protein		880	0
				S55507	protein disulfide-isomerase (EC 5.3.4.1) ER60 precursor		880	0
				BA003739.1	phospholipase C-alpha		871	0

5

10

15

158

			S6394	protein disulfide-isomerase (EC 5.3.4.1) ER60 precursor	867	0
			NP_004902.1	protein disulfide isomerase related protein (calcium-binding protein, intestinal-related)	340	4E-92
			NP_000909.2	(procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), beta polypeptide (protein disulfide isomerase, thyroid hormone binding protein p55), v-erb-a avian erythroblastic leukemia viral oncogene homolog 2-like)	250	6E-65
			CAA28775.1	prolyl 4-hydroxylase beta subunit (AA 1-491)	247	4E-64
			AAA61169.1	thyroid hormone binding protein precursor	245	1E-63
NM_016674	Mm.33669	F:2.65 (5m19)	NP_066924.1	claudin 1; senescence-associated epithelial membrane protein 1	316	4E-86
NP_057883.1			AAD22962.1	claudin-1	314	1E-85
			AAH01053.1	claudin 7	236	5E-62
			NP_001298.1	claudin 7; Clostridium perfringens enterotoxin receptor-like 2; claudin 9	234	2E-61
			XP_006547.1	similar to Claudin-19	219	3E-57
			NP_683763.1	claudin 19	218	1E-56
NM_008509	Mm.1514	F:2.64 (5m19)	NP_000228.1	lipoprotein lipase precursor	838	0
NP_032535.1			AAH11353.1	Similar to lipoprotein lipase	836	0
			AAC61679.1	lipoprotein lipase precursor	602	1E-170
			NP_006024.1	endothelial lipase precursor; endothelial cell-derived lipase	436	1E-120
			NP_000271.1	lipase C precursor	380	1E-103

5

10

15

20

159

			AAA59520.1	hepatic lipase precursor	379	1E-103
			A28997	triacylglycerol lipase (EC 3.1.1.3) precursor, hepatic	379	1E-103
NM_005690	Mm.6676	F:2.63 (7to19)	NP_005885.1	CD5 antigen-like (scavenger receptor cysteine rich family); Spalpa	517	1E-146
NP_033820.1			NP_015568.1	deleted in malignant brain tumors 1 isoform b precursor	277	4E-74
			CAB56155.1	DMBT1/8kb.2 protein	276	1E-73
			CAC44122.1	DMBT1/8kb.2 protein	275	2E-73
			NP_060049.1	deleted in malignant brain tumors 1 isoform c precursor	272	1E-72
			CAB63941.1	DMBT1 prototype	269	1E-71
			BAA78577.1	DMBT1	266	6E-71
			NP_004397.1	deleted in malignant brain tumors 1 isoform a precursor	263	5E-70
			S36077	M130 antigen	254	3E-67
			I38006	M130 antigen precursor, splice form 1	254	3E-67
			I38004	M130 antigen precursor, splice form 3	254	3E-67
			NP_004235.2	CD163 antigen; macrophage-associated antigen	254	3E-67
			AAF91396.1	scavenger receptor cysteine-rich type 1 protein M160 precursor	252	1E-66
			NP_542782.1	scavenger receptor cysteine rich domain containing, group B (4 domains); scavenger receptor cysteine-rich protein SRCRB-S4D	246	6E-65
			NP_005610.1	neutrophil precursor, protease, serine, 12, molopsin; brain-specific serine protease 3; leydin	226	9E-59
			AAH07761.1	protease, serine, 12 (neutrophil, molopsin)	208	3E-53
NM_025459	Mm.25311	F:2.63 (7to19)	IBAB15241.1	unnamed protein product	572	1E-163

5

10

15

20

160

NP_079735.1				NP_061873.2	hypothetical protein FLJ20152	571	1E-162
				BA490982.1	unnamed protein product	204	3E-52
				BAB15252.1	unnamed protein product	202	7E-52
X00496	Mm.7043	F:2.63 (5to19)		NP_004346.1	hypothetical protein FLJ13902	226	4E-59
CAA25191.1				HLHUG	class II histocompatibility antigen-associated gamma chain	226	4E-59
				CAA27047.1	gamma chain	225	9E-59
				P04233	HLA class II histocompatibility antigen, gamma chain (HLA-DR antigen associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD74 antigen)	207	1E-53
NM_011435	Mm.2407	F:2.61 (5to19)		NP_003093.1	superoxide dismutase 3, extracellular	288	6E-78
NP_035565.1							
NM_007574	Mm.3453	F:2.56 (5to19)		CHUQC	complement subcomponent C1q chain C precursor	270	3E-71
NP_031600.1				XP_031238.1	similar to pancreatic elastase (EC 3.4.21.36) IIIA precursor	269	4E-71
				BAB71575.1	unnamed protein product	268	1E-70
A K 0 0 4 3 8 7		F:2.55 (YtoO)		NP_036276	dynein, axonemal, intermediate polypeptide 1; dynein, axonemal, intermediate chain 1; dynein intermediate chain DNAH1	171	6E-43
BAC25081.1				AAF19816	dynein intermediate chain DNAH1	171	6E-43
				AAH30583	dynein, axonemal, intermediate polypeptide, 1	171	6E-43
NM_008330	Mm.24769	F:2.55 (5to19)		NP_062558.1	hypothetical protein R30953_1	228	1E-58

5

10

15

20

25

[illegible]

162

			XP_016076.2	similar to high mobility group 1	234	3E-61
			S30221	nucleosome chromosomal protein HMG-2B - human	233	9E-61
			XP_116482.1	similar to High mobility group protein 4 (HMG-4) (High mobility group protein 2a) (HMG-2a)	212	2E-54
			XP_063120.1	similar to high mobility group 1	212	2E-54
			XP_115897.1	similar to HMG2a (high mobility group protein 2a)	206	1E-52
			CAA22428.1	HMG2a (high mobility group protein 2a)	206	1E-52
			XP_089930.5	similar to high mobility group 1 protein	205	3E-52
X12905	Mm.8308	F2.51 (5019)	NP_002612.1	properdin P factor, complement	771	0
CAA31389.1			AAB62886.1	properdin	770	0
			S16150	properdin precursor - human.	768	0
			T45112	properdin [imported] - human	766	0
			T45113	properdin [imported] - human	764	0
			CAA15658.1	dJ212G6.2 (properdin)	731	0
			AAB63279.1	properdin	241	2E-63
			CAC37630.1	fibulin-6	236	7E-62
			AAK68690.1	hemiscentin	235	1E-61
			XP_053531.6	similar to hemiscentin	235	1E-61
			A05319	properdin - human (fragments).	196	7E-50
A R 007392	Mm.2131	F2.49 (5011)	S70439	pancreatic elastase 1 (allele HLE1.1-16) probable splice form I	426	1E-118

5

10

15

20



163

BAB25008.1				NP_001962.2	elastase 1, pancreatic	419	1E-116
				NP_254275.1	similar to elastase 1, pancreatic (H. sapiens)	278	7E-74
				BAA00165.1	pancreatic elastase 2 precursor	275	1E-72
				NP_056933.1	pancreatic elastase IIB	268	7E-71
				CAC2422.1	bA263F14.3 (Elastase 2B)	266	5E-70
				NP_031378.1	elastase 3B	253	3E-66
				P08861	Elastase IIB precursor (Protease E)	253	3E-66
				A29934	pancreatic elastase (EC 3.4.21.36) IIIA precursor	253	4E-66
				NP_005738.2	elastase 3, pancreatic (protease E)	252	6E-66
				P09093	Elastase IIIA precursor (Protease E)	252	6E-66
				AAA66350.1	elastase III A	251	2E-65
				AAH05918.1	Similar to elastase 3, pancreatic (protease E)	250	2E-65
				AAA36482.1	protease E precursor	250	3E-65
				S68826	pancreatic elastase (EC 3.4.21.36) isoform 2 precursor	241	1E-62
				Q99895	Caldeirin precursor (Chymotrypsin C)	241	1E-62
				NP_009203.1	chymotrypsin C (caldeirin); caldeirin (serum calcium decreasing factor, elastase IV)	240	2E-62
				CAA74031.1	chymotrypsin	236	3E-61
NM_016847	Mm.4351	E2.48 (5to19)		NP_000697.1	arginine vasopressin receptor 1A; V1a vasopressin receptor; vascular/hepatic-type arginine vasopressin receptor; antidiuretic hormone receptor 1A	701	0
NP_058543.1							

5

10

15

20

164

			NP_000698.1	arginine vasopressin receptor 1B; arginine vasopressin receptor 3; antidiuretic hormone receptor 1B; vasopressin Y1B receptor; pituitary vasopressin receptor 3	364	4E-99
			NP_000907.1	oxytocin receptor	355	2E-96
			1808301A	oxytocin receptor	355	2E-96
			CAA56562.1	oxytocin receptor	299	1E-79
			NP_000045.1	arginine vasopressin receptor 2	244	5E-63
			1913493A	vasopressin receptor:ISOTYPE-V2	241	3E-62
			AAB87678.1	vasopressin receptor type 2	216	1E-54
NM_053177	Mm.8356	F2.47 (7to19)	CAC08215.1	muco lipidin	1069	0
NP_444407			NP_063394.1	muco lipidin 1; muco lipidin	1069	0
			AAG4242.1	muco lipidin 1	998	0
			CAC07813.1	muco lipidin	679	0
			AAL34622.1	muco lipidin-3	628	1E-179
			NP_060768.7	muco lipidin-3	515	1E-145
NM_023733	Mm.28197	F2.47 (7to19)	Q9UKG9	Peroxisomal carnitine octanoyltransferase (COYT)	1118	0
NP_076222.1			JC7101	carnitine O-octanoyltransferase (EC 2.3.1.137)	1114	0
			NP_066974.1	carnitine O-octanoyltransferase	1114	0

5

10

15

20

165

				NP_000746.2	carbamate acetyltransferase precursor, isoform 1	305	3E-82
				NP_003994.2	carbamate acetyltransferase isoform 2	305	3E-82
				P43155	Carbamate O-acetyltransferase (Carbamate acetylase) (CAT)...	302	2E-81
AK007588	NULL	F:2.47 (5to7)		AAD30147.1	RING finger protein	214	9E-55
XP_135065.1				NP_055060.1	ring finger protein 7; sensitive to apoptosis gene	214	1E-54
NM_019985	Mm.30700	F:2.46 (7to19)		NP_057593.1	C-type lectin-like receptor-2	303	2E-82
NP_064369.1				AAH29554.1	Similar to C-type lectin-like receptor-2	248	6E-66
NM_007572	Mm.370	F:2.45 (5to19)		NP_057075.1	complement component 1, q subcomponent, alpha polypeptide precursor; complement C1q A chain precursor; complement component C1q A chain	286	2E-76
NP_031598.1							
A218416		F:2.44 (7to19)		NP_000361.1	tocopherol (alpha) transfer protein (ataxia (Friedreich-like) with vitamin E deficiency);	451	1E-126
AAF25956.1					Tocopherol (alpha) transfer protein		
				G01727	alpha-tocopherol transfer protein	449	1E-125
NM_019642	Mm.22130	F:2.41 (YtoM)		P04844	lithyl-diphosphooligosaccharide--protein glycosyltransferase 63 kDa subunit precursor (Ribophorin II) (RPN-II) (RIBIR)	1033	0
NP_062616.1				B26168	ribophorin II precursor	1032	0
				NP_002942.1	ribophorin II	1028	0
				AAH02380.1	Unknown (protein for IMAGE:2961244)	801	0

5

10

15

20

166

			AAH13028.1	Unknown (protein for IMAGE3532152)		480	1E-135
			CAC34517.1	dj343K2.2.3 (ribophorin II (isoform 3))		427	1E-119
NM_010442	Min.17980	E:2.41 (7to19)	AAH01491.1	heme oxygenase (deacylizing)		483	1E-136
NP_034572.1			NP_002124.1	heme oxygenase (deacylizing) 1		479	1E-135
			ptb1Q08	Chain A, X-Ray Crystal Structure Of Human Heme Oxygenase-1		375	1E-104
			NP_002125.3	heme oxygenase (deacylizing) 2		261	2E-69
			AAB22110.2	heme oxygenase-2; HO-2		255	1E-67
			SZ1700	heme oxygenase (deacylizing) (EC 1.4.99.3) 2		254	3E-67
			AAA50403.1	heme oxygenase		197	3E-50
NM_007833	Min.1987	E:2.41 (7to19)	NP_001911.1	decorin isoform a precursor; dermatan sulphate proteoglycan II; bone proteoglycan II; proteoglycan core protein		584	1E-156
NP_031859.1			AAA52301.1	decorin		554	1E-156
			NP_001702.1	biglycan preproprotein; bone/cartilage proteoglycan-1; dermatan sulphate proteoglycan 1		382	1E-105
			AAA52387.1	biglycan		366	1E-100
			NP_060150.2	asporin (LRR class 1); periodontal ligament associated protein 1		352	7E-96
			Q9BXN1	Asporin precursor (Periodontal ligament associated protein-1) (PLAP-1)		352	7E-96
			BAC04007.1	unnamed protein product		314	2E-84
			NP_598011.1	decorin isoform b precursor; dermatan sulphate proteoglycan II; bone proteoglycan II; proteoglycan core protein		303	5E-81
			NP_598012.1	decorin isoform c precursor; dermatan sulphate proteoglycan II; bone proteoglycan II; proteoglycan core protein		238	2E-61

5

10

15

20

167

				BAA90967.1	unnamed protein product	204	2E-51
NM_016850	Mm.3233	F:2.41 (5to19)		NP_004020.1	Interferon regulatory factor 7 isoform b	506	1E-143
NP_058546.1				NP_001563.2	Interferon regulatory factor 7 isoform a	505	1E-143
				Q92985	Interferon regulatory factor 7 (IRF-7)	505	1E-143
				NP_004022.1	Interferon regulatory factor 7 isoform d	503	1E-142
				AAB80691.1	putative interferon regulatory factor 7C.2	256	6E-68
NM_009777	Mm.2570	F:2.41 (5to19)		NP_000482.2	complement component 1, q subcomponent, beta polypeptide precursor, complement component C1q, B chain	288	9E-78
NP_033907.1				CHUQB	complement subcomponent C1q chain B precursor [validated]	288	9E-78
				P02746	Complement C1q subcomponent, B chain precursor	287	2E-77
				CAA26880.1	C1q B-chain precursor	277	2E-74
NM_008524		F:2.41 (5to19)		NP_002336.1	huminan	574	1E-162
NP_032550.1				AA485268.1	huminan	570	1E-161
				AAH35281.1	Similar to fibromodulin	292	2E-77
				Q06828	Fibromodulin precursor (FM) (Collagen-binding 59 kDa protein) (Keratan sulfate proteoglycan fibromodulin) (KSPG fibromodulin)	288	2E-76
				NP_002014.1	fibromodulin precursor	285	1E-75
				NP_008966.1	keratocan; cornea plana 2 (autosomal recessive)	220	4E-56

5

10

15

20

168

			NP_002716.1	proline arginine-rich end leucine-rich repeat protein	218	2E-55
			NP_005005.1	osteomodulin	211	3E-53
NM_010789	Mm.474	E:2.4 (5to19)	AAF81641.1	TALE homeobox protein Meis2d	749	0
NP_034919.1						
			O14770	Homeobox protein Meis2 (Meis1-related protein 1)	743	0
			NP_002389.1	Meis1 homolog; Meis1 (mouse) homolog	701	0
			AAF81639.1	TALE homeobox protein Meis2b	598	1E-170
			AAF81638.1	TALE homeobox protein Meis2a	591	1E-168
			iAAH01516.1	Unknown (protein for MCC-2820)	570	1E-162
			NP_064334.1	homeobox protein Meis2 isoform c; Meis (mouse) homolog 2; Meis1-related gene 1; TALE	456	1E-128
				homeobox protein Meis2		
			Q99687	Homeobox protein Meis3 (Meis1-related protein 2)	431	1E-120
			AAH25404.1	Similar to hypothetical protein DRFZp547H236	409	1E-113
			XP_085929.5	similar to Homeobox protein Meis3 (Meis1-related protein 2)	377	1E-104
			AAM09846.1	MEIS1-related protein 2	305	2E-82
NM_013485	Mm.29095	F:2.38 (5to19)	CAA6949.1	complement 9	665	0
NP_038513.1						
			NP_001728.1	complement component 9	665	0
			C9HU	complement C9 precursor [validated]	659	0
			AAA51839.1	C9 complement protein	652	0

5

10

15

20

169

			NP_000553.1	complement component 8, alpha polypeptide precursor	264	4E-70
			C8HUA	complement C8 alpha chain precursor [validated]	263	8E-70
NM_016906	Mm.28375	F:2.37 (5to19)	NP_037468.1	Sec61 alpha form 1; sec61 homolog	931	0
NP_058602.1			Q9Y2R3	Protein transport protein Sec61 alpha subunit isoform 2 (Sec61 alpha-2)	909	0
			NP_060614.2	sec61 homolog, Sec61 alpha form 2	891	0
			AAH02951.1	Similar to CG9539 gene product	828	0
			AAH26179.1	Similar to Sec61 alpha form 2	778	0
			BAB14148.1	unnamed protein product	775	0
			BAC11298.1	unnamed protein	696	0
			BAA91692.1	unnamed protein product	432	1E-121
			CAD38592.1	hypothetical protein	425	1E-119
			BAC11283.1	unnamed protein	338	2E-92
AK004979	Mm.33881	F:2.37 (5to19)	XP_091549.1	similar to RIKEN cDNA 1300010M03	801	0
BAB23715.1			BAB15241.1	unnamed protein product	236	2E-60
			BAC11332.1	unnamed protein product	226	1E-57
			NP_061873.2	hypothetical protein FLJ20152	208	3E-52

5

10

15

20

170

NM_013922	Min.103674	F:2.36 (7to19)	XP_094539	similar to zinc finger protein KID3	1145	0
NP_038950.1						
			AA069676	zinc finger protein KID3	1125	0
			T46469	hypothetical protein DKFZp434G1930.1	699	0
NM_009369	Min.14455	F:2.36 (5to11)	NP_000349.1	transforming growth factor, beta-induced, 68kDa; corneal dystrophy, kerato-epithelial;	1144	0
NP_033951.1				transforming growth factor, beta-induced, 68kD		
			AAC08449.1	BIGH3	905	0
			AA017733.1	extracellular matrix protein perostin-bm	571	1E-162
			NP_006466.1	osteoblast specific factor 2 (hscichn 1-like); perostin	568	1E-161
			S36111	osteoblast-specific factor 2	568	1E-161
			AAC24944.1	BIGH3	332	2E-90
NM_022309	Mm.2018	F:2.36 (5to19)	NP_074036.1	core-binding factor, beta subunit, isoform 1; poliovirus enhancer binding protein 2, beta subunit; SL2.3 enhancer factor 1 beta subunit; SL3/AKV core-binding factor beta subunit	344	5E-94
NP_071704.1						
			NP_001746.1	core-binding factor, beta subunit, isoform 2; poliovirus enhancer binding protein 2, beta subunit; SL2.3 enhancer factor 1 beta subunit; SL3/AKV core-binding factor beta subunit	302	2E-81
				transcription factor CBF beta - human	287	5E-77
			I59579		287	5E-77
			pdh1/CL3	Chain A, Molecular Insights Into Pebp2CBF-Smmtic Associated Acute Leukemia Revealed From The Three-Dimensional Structure Of Pebp2CBF BETA		
			pdh1/H9D	Chain A, AmTCBF-BeadDNA COMPLEX	278	4E-74
A K 0 1 8 5 8 5	Mm.97986	F:2.35 (5to19)	NP_079282.1	hypothetical protein FLJ13373	543	1E-153
BAB1292.1						
			CAD39164.1	hypothetical protein	543	1E-153

5

10

15

20



171

NM_013594	Mm.22522	E2.35 (5to19)	AAD50371.1	methyl-CpG binding protein 1	779	0
NP_038622.1			NP_056671.2	methyl-CpG binding domain protein 1 isoform 1	779	0
			AAD51442.1	methyl-CpG binding protein splice variant 1	773	0
			NP_056670.2	methyl-CpG binding domain protein 1 isoform 2	662	0
			AAD51443.1	methyl-CpG binding protein splice variant 2	657	0
			NP_056723.2	methyl-CpG binding domain protein 1 isoform PCM1	632	1E-179
			CAA71735.1	methyl-CpG binding protein	625	1E-177
			AHH33242.1	methyl-CpG binding domain protein 1	597	1E-169
			NP_056669.1	methyl-CpG binding domain protein 1 isoform 3	596	1E-169
			NP_002375.1	methyl-CpG binding domain protein 1 isoform 4	526	1E-148
			AAH12487.1	Unknown (protein for MGC:21089)	263	1E-68
Z35168	Mm.155579	E2.34 (Ynm4)	CAB90289.1	6A24A23.1 (collagen, type IV, alpha 5 (Alport syndrome))	476	1E-134
CAA84531.1			NP_203699.1	alpha 5 type IV collagen, isoform 2, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	476	1E-134
			AAAS1558.1	alpha-5 type IV collagen	476	1E-134
			NP_000486.1	alpha 5 type IV collagen, isoform 1, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	476	1E-134
			AAAS9480.1	alpha-5 type IV collagen	476	1E-134
			NP_203700.1	alpha 5 type IV collagen, isoform 3, precursor; collagen IV alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	476	1E-134

5

10

15

20

172

	AAA52045.1	collagen type IV alpha 5 chain	476	1E-134
	CAC3153.1	bA72K172 (collagen type IV alpha 1)	421	1E-118
	AAA52066.1	pro-alpha-1(IV)	421	1E-118
	AAH47305.1	Similar to collagen, type IV, alpha 1	421	1E-118
	AAA52042.1	procollagen alpha-1 type IV	421	1E-118
5	NP_001836.1	alpha 1 type IV collagen preproprotein; collagen IV, alpha-1 polypeptide; collagen of basement membrane, alpha-1 chain	421	1E-118
	IL11A	Chain A, The 1.9-A Crystal Structure Of The Noncollagenous (Nc1) Domain Of Human Placenta Collagen Iv Shows Stabilization Via A Novel Type Of Covalent Met-Lys Cross-Link.	419	1E-117
	1402236A	collagen alpha1 (IV)	417	1E-117
	AAM97359.1	arrestin	415	1E-116
	NP_000082.1	alpha 3 type IV collagen, isoform 1, precursor; collagen IV, alpha-3 polypeptide (goodpasture antigen)	365	1E-101
10	COHU3B	collagen alpha 3 (IV) chain precursor, long splice form	365	1E-101
	CAC36101.1	alpha3 type IV collagen	365	1E-101
	AAA51566.1	alpha-3 type IV collagen	365	1E-101
	AAA21610.1	alpha-3 type IV collagen	365	1E-101
	AAF72632.1	tuustatin	365	1E-101
15	AAB19637.1	type IV collagen alpha 3 chain	351	5E-97
	CAA29098.1	alpha (2) chain	318	6E-87
	P08572	Collagen alpha 2 (IV) chain precursor	318	6E-87
	NP_001837.1	alpha 2 type IV collagen preproprotein; canstatin	318	6E-87
20	IL11C	Chain C, The 1.9-A Crystal Structure Of The Noncollagenous (Nc1) Domain Of Human Placenta Collagen Iv Shows Stabilization Via A Novel Type Of Covalent Met-Lys Cross-Link.	318	6E-87
	AAA52043.1	alpha-2 type IV collagen	317	1E-86
	AAA58422.1	collagen alpha-2 type IV	316	2E-86
	AAF72631.1	canstatin	316	2E-86
	NP_378667.1	type IV alpha 6 collagen, isoform B precursor; collagen IV, alpha-6 polypeptide; collagen of basement membrane, alpha-6	308	4E-84
25	AAB19039.1	collagen type IV alpha chain	308	4E-84
	Q14031	Collagen alpha 6 (IV) chain precursor	308	4E-84
	AAB19038.1	collagen type IV alpha chain	308	4E-84

173

				NP_001838.1	type IV alpha 6 collagen, isoform A precursor; collagen IV, alpha-6 polypeptide; collagen of basement membrane, alpha-6 collagen	308	4E-34
				BAA04809.1	collagen	308	4E-34
				NP_000083.1	alpha 4 type IV collagen precursor; Collagen IV, alpha-4 polypeptide; collagen of basement membrane, alpha-4 chain	286	2E-77
				BAA04214.1	alpha 4(IV) collagen	286	2E-77
				Bt9736	collagen alpha 3(IV) chain, medium splice form - human	233	2E-61
				AAA18942.1	collagen type IV alpha 3	233	2E-61
				NP_112730.1	alpha 3 type IV collagen, isoform 2, precursor; collagen IV, alpha-3 polypeptide (goodpasture antigen)	233	2E-61
NM_010906	Mm.9394	F.234 (YtoM)		NP_002492	nuclear factor I/X (CCAAT-binding transcription factor)	738	0
NP_035036.1				AAB52369	nuclear factor I	719	0
				AAB52371	nuclear factor I	692	0
				Q14938.	Nuclear factor 1 X-type (Nuclear factor 1/X) (NF1-X) (NF1-X) (C/CAAT-box binding transcription factor) (CTF) (TGGCA-binding protein).	692	0
				XP_046627	Similar to transcription factor NF1 (Rattus norvegicus)	524	1E-148
				Q12857	Nuclear factor 1-A-type (Nuclear factor 1/A) (NF1-A) (NF1-A) (C/CAAT-box binding transcription factor) (CTF) (TGGCA-binding protein).	524	1E-148
				BAA92677	KIAA1439 protein	524	1E-148
				P08651	Nuclear factor 1 C-type (Nuclear factor 1/C) (NF1-C) (NF1-C/NFI-C) (C/CAAT-box binding transcription factor) (CTF) (TGGCA-binding protein).	429	1E-120
				AAH12120	nuclear factor I/G (CCAAT-binding transcription factor)	428	1E-120
				NP_005588	nuclear factor I/C (CCAAT-binding transcription factor)	427	1E-119
				B33416.	nuclear factor I	426	1E-119
				S01038	transcription factor, CCAAT-binding	416	1E-116
				AA093126	nuclear factor 1 X-type	410	1E-114
				AAH01283	Similar to nuclear factor I/B	410	1E-114
				NP_005587	nuclear factor I/B	409	1E-114
				AAC15752	NF1-X_HUMAN NUCLEAR FACTOR 1/X (NF1-X); CCAAT-BOX BINDING TRANSCRIPTION FACTOR (CTF); TGGCA-BINDING PROTEIN	390	1E-108

5

10

15

20

25

174

			AA493124	nuclear factor 1 A-type	389	1E-107
			AAD38240	nuclear factor 1-X (AA 187-441); nuclear factor 1X; NF1X_HUMAN NUCLEAR FACTOR 1X;	354	2E-97
				NFL-X; NF-1X; TGCCA-BINDING PROTEIN; CTF		
			AA493125	nuclear factor 1 B-type	352	7E-97
			AAB51197	nuclear factor 1B3	350	4E-96
			AAC32593	CTF5	343	3E-94
			AAC32594	CTF-1	331	2E-90
			AAD38241	NFL-X3=transcription factor	307	3E-83
			AAB32370	nuclear factor 1	216	6E-56
			NP_005561.1	lectin, mannose-binding, 1 precursor; intracellular mannose specific lectin; endoplasmic	849	0
			F2.34 (5to19)	reticulum-golgi intermediate compartment protein 53		
			S42626	ER-golgi intermediate compartment protein	848	0
			AAH32330.1	lectin, mannose-binding, 1	848	0
			I919261A	protein ERGIC-53	844	0
			NP_068591.1	lectin, mannose-binding, 1 like; ERGL protein, ERGIC-53-like protein	255	2E-66
			NP_000168.1	gelsolin (anyloidsosis, Finnish type); Gelsolin	1422	0
			F2.34 (5to19)			
			Q9Y6U3	Adseverin (Scinderin)	904	0
			BAC11416.1	unnamed protein product	904	0
			AAK60494.1	scinderin	899	0
			NP_009058.1	villin 1; Villin-1	672	0
			AAD15423.1	similar to mouse adseverin(DS); similar to PID-g218019	666	0
			BAB67798.1	KIAA1905 protein	666	0
			pdbj DB0	Chain A, Carboxy-Terminal Half Of Gelsolin (G4-G6) Bound To Actin	643	0

5

10

15

20

25

175

			NP_006567.2	advillin		640	0
			O75366	Advillin (p92)		638	0
			NP_149119.1	scinderin; adaeverin; KIAA1905 protein		588	1E-167
			AAH17491.1	Similar to gelsolin (amyloidosis, Finnish type)		542	1E-153
			BAC11465.1	unnamed protein product		497	1E-139
			AAH04134.1	Similar to advillin		464	1E-129
			pdbj1JHW	Chain A, Ca2+-Binding Mimicry In The Crystal Structure Of The Eu3+-Bound Mutant Human Macrophage Capping Protein Cap G		389	1E-106
NM_010238	Mm.3444	F:2.33 (7to19)	NP_005095.1	bromodomain containing protein 2; female sterile homeotic-related gene 1		1083	0
NP_034368.1			CAC69991.1	O14.1.1 (bromodomain-containing protein 2 (RING3, KIAA9001), isoform 1)		1082	0
			A56619	female sterile homeotic (fsh) homolog RING3		1048	0
			CAA65430.1	kinase		1046	0
			NP_031397.1	bromodomain containing protein 3; bromodomain-containing 3; RING3-like gene; open reading		642	0
			AAC27978.1	frame X R31546_1		577	1E-164
			NP_490597.1	bromodomain-containing protein 4 isoform long; similar to RING3; chromosome-associated protein		577	1E-164
			NP_055114.1	bromodomain-containing protein 4 isoform short; similar to RING3; chromosome-associated protein		577	1E-164
			NP_001717.1	testis-specific bromodomain protein		506	1E-142
			AAH32124.1	Similar to bromodomain containing 3		484	1E-136

5

10

15

176

NM_013521	Mm.56951	F2.33 (5to19)	A42009	N-formyl peptide receptor		540	1E-133
NP_038549.1			NP_002020.1	formyl peptide receptor 1		538	1E-133
			P21462	[Met-Leu-Phe receptor (FMLP receptor) (N-formyl peptide receptor) (FPR) (N-formyl peptide chemoattractant receptor)		537	1E-133
			AAA36362.1	N-formyl peptide receptor FMLP-R98		535	1E-132
			NP_001453.1	formyl peptide receptor-like 1; lipoxin A4 receptor (formyl peptide receptor related)		451	1E-127
			AAA58481.1	FMLP-related receptor II		450	1E-126
			XP_009373.1	similar to N-formyl peptide receptor-like 2 protein		377	1E-104
			NP_002021.2	formyl peptide receptor-like 2		374	1E-103
			AAC51258.1	orphan G-protein coupled receptor Der isoform a		227	2E-59
			Q99788	Chemokine receptor-like 1 (G-protein coupled receptor DEZ) (G protein-coupled receptor GlemR23)		224	2E-58
			NP_004063.1	chemokine-like receptor 1		224	2E-58
			NP_001727.1	complement component 5 receptor 1 (C5a ligand); complement component-5 receptor-2 (C5a ligand)		203	4E-52
			1705295A	anaphylatoxin C5a chemotactic receptor		203	4E-52
A K 0 2 0 8 8 1	Mm.42222	F2.32 (YcoM)	NP_009055	utrophin; dystrophin-related protein		303	2E-52
BAB32239.1							
NM_019630	Mm.27545	F2.32 (7to19)	AAF62893.1	protein arginine N-methyltransferase 1-variant 2		710	0
NP_062804.1			Q99873	Protein arginine N-methyltransferase 1 (interferon receptor 1-bound protein 4)		707	0

5

1.0

15

20

177

		AAF62895.1	protein arginine N-methyltransferase 1-variant 1	673	0
		AAF62894.1	protein arginine N-methyltransferase 1-variant 3	673	0
		CAA71765.1	arginine methyltransferase	670	0
		CAA71763.1	arginine methyltransferase	670	0
		NP_001577.1	HMT1 hnRNP methyltransferase-like 2	637	0
		Q9NR22	Protein arginine N-methyltransferase 4	562	1E-160
		NP_062838.2	HMT1 hnRNP methyltransferase-like 3	562	1E-160
		AAH19339.1	Unkzova (protein for IMAGE3027997)	296	4E-80
		O60678	Protein arginine N-methyltransferase 3	296	4E-80
A F 3 2 0 9 6	Mm.14569	NP_057712.2	WW domain-containing adapter with a coiled-coil region isoform 1	1044	0
AAK73808.1		NP_567822.1	WW domain-containing adapter with a coiled-coil region, isoform 2	931	0
		BAB71029.1	unnamed protein product	949	0
		AAH04238.1	hypothetical protein PRO1741	938	0
		CAC16000.1	bA48B24.1 (A novel protein containing a formin binding protein (FBP28) domain)	861	0
		CAD28517.1	hypothetical protein	588	1E-167
		BAB47473.1	KIAA1844 protein	533	1E-150
		NP_567823.1	WW domain-containing adapter with a coiled-coil region, isoform 3	521	1E-146

5

10

15

178

			AAH10356	hypothetical protein MGC10753	350	5E-95
NM_020564	Mm.6562	F:2.32 (31019)	AAC78553.1	hydroxysteroid sulfotransferase SUL72B1a	228	1E-59
NP_065589.1			NP_004596.1	sulfotransferase family, cytosolic, 2B, member 1; sulfotransferase family 2B, member 1	228	1E-59
			AAC78499.1	hydroxysteroid sulfotransferase SUL72B1b	228	1E-59
			21465697	Chain A, Crystal Structure Of Human Dehydroepiandrosterone Sulfotransferase In Complex With Substrate	218	1E-56
NM_007614	Mm.3476	F:2.31 (YtoM)	NP_001895.1	catenin (cadherin-associated protein), beta 1, 88kDa; catenin (cadherin-associated protein), beta 1 (88kD); catenin (cadherin-associated protein), beta 1 (88kDa)	1523	0
NP_031640.1			pdbj1JPW	Chain A, Crystal Structure Of A Human Tcf-4 BETA-Catenin Complex	1026	0
			pdbj1G3J	Chain A, Crystal Structure Of The XctB-ChdBETA-Catenin Armadillo Repeat Complex	1014	0
			pdbj1JDH	Chain A, Crystal Structure Of Beta-Catenin And Hicf-4	1007	0
			BAB93475.1	catenin beta 1	994	0
			AAH00441.1	junction plakoglobin	929	0
			NP_002221.1	junction plakoglobin, isoform 1; gamma-catenin	929	0
			P14923	Junction plakoglobin (Desmoplakin III)	913	0
			AAAG4895.1	Plakoglobin	912	0
			AA189457.1	beta-catenin	612	1E-174
			2121362A	plakoglobin	293	1E-77

5

10

15

20



212

NM_008015	Mm.18459	F:2.14 (5019)	AAC34298.1	DEAD box RNA helicase DDX3	984	0
NP_032041.1			AAC51829.1	dead box, X isoform	983	0
			NP_004651.2	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide, Y chromosome; DEAD/H box-3, Y-linked	931	0
			O15523	DEAD-box protein 3, Y-chromosomal	928	0
			AAF72705.1	VASA protein	439	1E-121
			CAB70750.1	hypothetical protein	439	1E-121
			XP_066968.2	similar to DEAD (aspartate-glutamate-alanine-aspartate) box polypeptide 3; D-E-A-D (aspartate-glutamate-alanine-aspartate) box polypeptide 3; embryonic RNA helicase	404	1E-121
			AAF66385.1	DEAD box RNA helicase	437	1E-121
A E 0 0 8 5 9 0	Mm.33403	F:2.14 (5019)	P49961	Ectonucleoside triphosphate diphosphohydrolase 1 (NTPDase1) (Ecto-ATP diphosphohydrolase (ATPDase) (Lymphoid cell activation antigen) (Ecto-apyrase) (CD39 antigen)	241	2E-62
BAB25764.1			NP_001767.2	ectonucleoside triphosphate diphosphohydrolase 1; CD39 antigen	241	2E-62
			Q9Y5L3	Ectonucleoside triphosphate diphosphohydrolase 2 (NTPDase2) (Ecto-ATPase) (CD39 antigen-like 1)	231	3E-59
			NP_001239.1	ectonucleoside triphosphate diphosphohydrolase 3; CD39-like 3	229	1E-58
			AAC09236.2	E-type ATPase	229	1E-58
NM_009895	Mm.4592	F:2.13 (YtoO)	NP_659508	cytokine-inducible SH2-containing protein isoform 2; cytokine-inducible SH2-containing protein; cytokine-inducible inhibitor of signaling type 1B; suppressor of cytokine signaling	469	1E-137
NP_034025.1			NP_037456	cytokine-inducible SH2-containing protein isoform 1; cytokine-inducible SH2-containing protein; cytokine-inducible inhibitor of signaling type 1B; suppressor of cytokine signaling	456	1E-128
			AAF97410	cytokine-inducible inhibitor of signalling type 1b	456	1E+128

5

10

15

20

211

			IC5695	Dnm1p/Vps1p-like protein		1256	0
			AAH00136.1	Similar to dynamin 1-like		1211	0
			A40671	dynamin, internal form 1, long C-terminal form		456	1E-126
			B40671	dynamin, internal form 2, short C-terminal form		456	1E-126
			NP_004399.1	dynamin 1; dynamin; dynamin1; Dynamin-1		456	1E-126
			IC4505	dynamin II - human		441	1E-122
			P50570	Dynamin 2		440	1E-122
			NP_004936.1	dynamin 2; Dynamin II		439	1E-121
			BAA74843.2	KIAA0820 protein		429	1E-118
			XP_044463.5	similar to Dynamin 3 (Dynamin, testicular) (T-dynamin)		429	1E-118
			NP_056384.1	KIAA0820 protein		428	1E-118
			CAB92724.1	ba277/Ci4.1 (novel Dynamin family member (KIAA0820))		324	1.5E-86
NM_013562	Mm.168	F2.15 (5to19)	6162421	similar to INTERFERON-RELATED DEVELOPMENTAL REGULATOR 1 (NERVE GROWTH FACTOR-INDUCIBLE PROTEIN PC4)		819	0
NP_038590.1			7387801	INTERFERON-RELATED DEVELOPMENTAL REGULATOR 1 (NERVE GROWTH FACTOR-INDUCIBLE PROTEIN PC4)		816	0
			4594607	interferon-related developmental regulator 1		774	0
			AAC24562.1	similar to mouse interferon-related protein PC4; 96% identical to P19182 (PID:g135861)		516	1E-146
			Q12894	Interferon-related developmental regulator 2 (SKMC15 protein)		409	1E-114
			AAC16924.1	interferon-related putative protein		409	1E-114
			NP_006755.2	interferon-related developmental regulator 2; Interferon-related protein		409	1E-114
			AAH01327.1	interferon-related developmental regulator 2		407	1E-113

5

10

15

20

## 210

				CAA23782.1	histocompatibility antigen HLA-DR	214	2E-55
				I72480	MHC cell surface glycoprotein	204	1E-52
				I54437	MHC class II DQ-alpha protein - human (fragment)	199	4E-51
				I68717	gene HLA-DQA2 protein - human (fragment)	197	1E-50
A K 0 0 8 2 7 3	Mm.2241	F2.15 (7to19)		NP_001166.1	Rho GDP dissociation inhibitor (GDI) beta, Ly-GDI	270	3E-71
XP_122918.1				pdcl DS6	Ras-Related C3 Botulinum Toxin Substrate 2	267	2E-70
				CAA45344.1	Rho GDP dissociation inhibitor (GDI)	234	1E-60
				NP_004300.1	Rho GDP dissociation inhibitor (GDI) alpha	234	2E-60
				pdcl FST	Chain A, Crystal Structure Of Truncated Human RhoGdi Triple Mutant	231	1E-59
				pdcl FT0	Chain A, Crystal Structure Of Truncated Human RhoGdi K113a Mutant	226	6E-58
				pdcl FT3	Chain A, Crystal Structure Of Truncated RhoGdi K141a Mutant	226	6E-58
				pdcl RHO	Chain A, Structure Of Rho Guanine Nucleotide Dissociation Inhibitor	223	3E-57
				pdcl FSO	Chain A, Crystal Structure Of Truncated Human RhoGdi Quadruple Mutant	223	3E-57
A K 0 1 8 1 9 5	Mm.140013	F2.15 (5to19)		NP_005681.1	dynamitin 1-like protein, isoform 3; dynamitin-like protein	1274	0
BAC38054.1				AAH24590.1	dynamitin 1-like	1270	0
				NP_036193.1	dynamitin 1-like protein, isoform 2; dynamitin-like protein	1269	0
				BAA22193.1	Dnm1p/Vps1p-like protein	1260	0
				AA039541.1	dynamitin-like protein DYNIV-11	1260	0
				NP_036192.1	dynamitin 1-like protein, isoform 1; dynamitin-like protein	1259	0

5

10

15

20

209

		NP_002110.1	major histocompatibility complex, class II, DO alpha; lymphocyte antigen; HLA-DQ-alpha; major histocompatibility complex, class II, DN alpha	252	7E-67
		BAA81787.1	HLA-DNA1.1a	247	2E-65
		XP_042473.2	major histocompatibility complex, class II, DR alpha precursor	245	8E-65
		AAA36501.1	hla-dr antigen heavy chain (aa 3 at 60)	245	8E-65
		CAA25076.1	HLA-DR alpha heavy chain	245	8E-65
		NP_061984.1	major histocompatibility complex, class II, DR alpha precursor; HLA class II histocompatibility antigen, DR alpha chain	244	2E-64
		AAB70189.1	MHC class II antigen DQ-alpha-1 chain	240	2E-63
		1102205B	antigen HLA Dalpha	235	8E-62
		pdb 1AQD	Chain A, Hla-Drl (Dra, Db1 0101) Human Class II Histocompatibility Protein (Extracellular Domain) Complexed With Endogenous Peptide	231	2E-60
		pdb 1A6A	Chain A, The Structure Of An Intermediate In Class II Mhc Maturation: Clip Bound To Hla-Df3	220	2E-57
		pdb 1EX2	Chain A, Crystal Structure Of Hla-Df2 (Dra0101,Db11501) Complexed With A Peptide From Human Myelin Basic Protein	220	2E-57
		pdb 1KG0	Chain A, Structure Of The Epstein-Barr Virus Gp42 Protein Bound To The Mhc Class II Receptor Hla-Drl	220	2E-57
		pdb 18H	Chain A, Crystal Structure Of A Complex Of A Human AlphaBETA-T Cell Receptor, Influenza Hs Antigen Peptide, And Mhc Class II Molecule, Hla-Df4	220	2E-57
		pdb 1HXY	Chain A, Crystal Structure Of Staphylococcal Enterotoxin II In Complex With Human Mhc Class II	220	2E-57
		pdb 1KLG	Chain A, Crystal Structure Of Hla-DrlTP(23-37, Thr28->ile Mutant) Complexed With Staphylococcal Enterotoxin C3 Variant 3b2 (Sec3-3b2)	220	2E-57
		pdb 1KLU	Chain A, Crystal Structure Of Hla-DrlTP(23-37) Complexed With Staphylococcal Enterotoxin C3 Variant 3b2 (Sec3-3b2)	220	2E-57
		1102205A	antigen HLA Dalpha	214	1E-55

5

10

15

208

			AAC41957.1	MHC class II HLA-DQ-alpha chain	318	7E-87
			AAC41956.1	MHC class II HLA-DQ-alpha chain	315	6E-86
			AAC41958.1	MHC class II HLA-DQ-alpha chain	312	5E-85
			AAC41955.1	MHC class II HLA-DQ-alpha chain	312	5E-85
			AAC41951.1	MHC class II HLA-DQ-alpha chain	311	1E-84
			AAC41950.1	MHC class II HLA-DQ-alpha chain	310	2E-84
			AAC41962.1	MHC class II HLA-DQ-alpha chain	310	2E-84
			AAC41953.1	MHC class II HLA-DQ-alpha chain	308	6E-84
			AAA85334.1	HLA-DQ alpha chain	308	1E-83
			AAC41954.1	MHC class II HLA-DQ-alpha chain	306	3E-83
			AAC41961.1	MHC class II HLA-DQ-alpha chain	300	3E-81
			AAC41959.1	MHC class II HLA-DQ-alpha chain	299	5E-81
			AAA59774.1	MHC HLA-DQ-alpha precursor	293	2E-79
			CAC88114.1	MHC class II antigen	289	4E-78
			polb1JK8	Chain A, Crystal Structure Of A Human Insulin Peptide-HLA-Dp8 Complex	280	2E-75
			XP_165698.1	similar to HLA class II histocompatibility antigen, DP alpha chain precursor (HLA-SB alpha chain) (MHC class II DP3-alpha) (DP(W3)) (DP(W4))	273	3E-73
			NP_291032.1	major histocompatibility complex, class II, DP alpha 1; HLA class II histocompatibility antigen, DP alpha chain	273	4E-73
			CAA25143.1	SB classII histocompatibility antigen alpha- chain	258	7E-69

207

NP_034508.1				MHC class II histocompatibility antigen HLA-DQ alpha chain precursor	347	1E-95
	A29312			antigen alpha,II histocompatibility	346	3E-95
	1004300B			MHC class II histocompatibility antigen HLA-DQ alpha 1 (DQw4 specificity) precursor	345	7E-95
	A37044			HLA class II histocompatibility antigen, DQ(2) alpha chain precursor	344	1E-94
	P04236			major histocompatibility complex, class II, DQ alpha 1 precursor	343	2E-94
	NP_002113.2			MHC class II antigen precursor	343	2E-94
	AAK11577.1			HLA class II histocompatibility antigen, DQ(5) alpha chain precursor (DC-1 alpha chain)	341	1E-93
	P01907			antigen alpha,II histocompatibility	340	1E-93
	1004300C			MHC HLA-DQA1-alpha protein	340	2E-93
	AAA52671.1			HLA class II histocompatibility antigen, DQ(1) alpha chain precursor (DC-4 alpha chain)	339	3E-93
	P01908			major histocompatibility complex, class II, DQ alpha 2	338	9E-93
	NP_064440.1			MHC class II HLA-DQ-alpha chain	337	1E-92
	AAB51233.1			MHC HLA-DX-alpha chain	337	2E-92
	AAA59834.1			MHC class II histocompatibility antigen HLA-DQ alpha 2 chain	337	2E-92
	HLHUDX			cell surface glycoprotein - human	333	2E-91
	I54290			HLA class II histocompatibility antigen, DQ(W3) alpha chain precursor	331	8E-91
	P05536			similar to HLA class II histocompatibility antigen, DQ(3) alpha chain precursor (DC-alpha)	331	8E-91
	XP_175260.1			(HLA-DCA) (HLA-DQA1*0501)		
	AAA69564.1			HLA DQA*0302	325	5E-89
	AAA59754.1			HLA-DQ alpha chain	325	5E-89
	P04225			HLA class II histocompatibility antigen, DQ(4) alpha chain precursor (DQ-DRW9 alpha chain)	323	2E-88
	I54444			MHC HLA-DQ-alpha chain precursor old gene name 'HLA-DQA'	320	2E-87
	I61294A			HLA DQw4 alpha	318	6E-87

5

10

15

20

206

NM_011415	Mm.4272	F:2.16 (5to11)	NP_003039.1	snail 2, neural crest transcription factor SLUG; slug (chicken homolog), zinc finger protein	458	1E-128
NP_035545.1			NP_005976.2	snail 1 homolog; snail 1 zinc finger protein	248	2E-65
			AAD17332.1	zinc finger protein	248	2E-65
			XP_065615.1	similar to snail 1 (drosophila homolog), zinc finger protein	211	4E-54
A.K.011306	Mm.196607	F:2.16 (5to19)	NP_001961.1	eukaryotic translation initiation factor 5A; eIF5A; eIF5A	311	1E-83
BAB27332.1			I53801	gene eIF-5A protein	302	6E-81
			XP_016093.1	similar to eukaryotic translation factor 5A	300	1E-80
			NP_065123.1	eIF-5A2 protein; eIF5AII	265	1E-69
NM_007686	Mm.117180	F:2.16 (5to19)	CAA68416.1	factor I	832	0
NP_031712.1			*			
			P05156 *	Complement factor I precursor (C3B/C4B inactivator)	832	0
			NP_000195.1	I factor (complement)	830	0
			*			
			AAH20718.1	Similar to I factor (complement)	434	1E-120
			CAA68417.1	heavy chain of factor I	472	1E-117
			CAA68418.1	light chain of factor I	414	1E-114
			I202205A	complement factor I light chain	328	2E-88
NM_010378	Mm.175310	F:2.15 (11to19)	HLHUDC	MHC class II histocompatibility antigen HLA-DC4 alpha chain precursor	347	1E-95

5

10

15

20

## 205

			JN0619	glucuronosyltransferase (EC 2.4.1.17) 2B-4 precursor		702	0
			AAC3272.1	UDP glucuronosyltransferase 2B4 precursor		697	0
			NP_001065.1	UDP glycosyltransferase 2 family, polypeptide B7; UDP-glucuronosyltransferase, family 2, beta-7		692	0
			S1309	glucuronosyltransferase (EC 2.4.1.17)		691	0
			AAH30974.1	UDP glycosyltransferase 2 family, polypeptide B7		690	0
			NP_066962.1	UDP glycosyltransferase 2 family, polypeptide B4; UDP-glucuronosyltransferase, family 2, beta-4		688	0
			NP_001064.1	UDP glycosyltransferase 2 family, polypeptide B11		677	0
			J20200	orphan UDP-glucuronosyltransferase (EC 2.4.-.-)		677	0
			NP_001066.1	UDP glycosyltransferase 2 family, polypeptide B10		660	0
			NP_444267.1	UDP glycosyltransferase 2 family, polypeptide B28		660	0
			NP_066789.1	UDP glycosyltransferase 2 family, polypeptide A1; UDP glucuronosyltransferase 2 family, polypeptide A1		579	1E-165
NM_015784	Mm.10681		NP_006466	osteoblast specific factor 2 (fascilin I-like), periostin		1423	0
NP_056599.1	F2.17 (YnoO)		AAH17733	extracellular matrix protein periostin-bm		1379	0
			S36111	osteoblast-specific factor 2		1372	0
			NP_000349	transforming growth factor, beta-induced, 68kDa; corneal dystrophy, kerato-epithelin; transforming growth factor, beta-induced, 68kD		580	1E-165
			AAC08449	BIGHE3		497	1E-140
AK007710	Mm.27385		NP_079012.1	hypothetical protein FLJ12150		463	1E-129
BA025204.1	F2.17 (3to19)		AAG22861.1	FKSG10		341	1E-95



204

			NP_073155.1	extracellular matrix protein 1, isoform 2 precursor; secretory component p85	301	3E-80
NM_010078	Mm.88188	E2.18 (Sto19)	000571	DEAD-box protein 3 (Helicase-like protein 2) (HLP2) (DEAD-box, X isoform)	1038	0
NP_034158.1			NP_001347.2	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3; DEAD/H box-3; helicase like protein 2; CAP-RF	1036	0
			NP_004651.2	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide, Y chromosome; DEAD/H box-3, Y-linked	968	0
			O15523	DEAD-box protein 3, Y-chromosomal	966	0
			NP_061912.1	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 4; VASA protein	441	1E-123
			T46407	probable RNA helicase protein DKFZp434B1122.1	441	1E-123
			AAF86585.1	DEAD box RNA helicase	439	1E-123
			XP_006968.2	similar to DEAD (aspartate-glutamate-alanine-aspartate) box polypeptide 3; D-E-A-D (aspartate-glutamate-alanine-aspartate) box polypeptide 3; embryonic RNA helicase	393	1E-108
			NP_006377.1	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 17 isoform 1; DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 17 (72kD); probable RNA-dependent helicase p72	322	3E-87
			1406327A	growth regulated nuclear 68 protein	315	2E-85
NM_053215	Mm.160362	E2.18 (Sto19)	NP_001068.1	UDP-glucosyltransferase 2 family, polypeptide B17; UDP-glucuronyltransferase, family 2, beta-17	728	0
NP_444445.1			XP_011097.5	similar to UDP-glucuronosyltransferase 2B15 precursor, microsomal (UDP-GT) (UDPGT1H-3) (HLUG4)	715	0
			NP_001067.1	UDP-glucosyltransferase 2 family, polypeptide B15; UDP-glucuronosyltransferase, family 2, beta-15	715	0
			AA055093.1	UDP-glucuronosyltransferase 2B15	712	0
			XP_050345.4	similar to UDP-glucuronosyltransferase 2B4 precursor, microsomal (UDPGT) (Hydroxyxychoic acid) (HLUG25) (UDPGT1H-1)	705	0
			AA055002.1	UDP-glucuronosyltransferase 2B4 precursor	703	0

203

			NP_000887.1	cytochrome P450, subfamily IVF, polypeptide 3; leukotriene B4 20-monooxygenase; cytochrome P450-17B-omega	808	0
			Q9HCS2	Cytochrome P450 4F12 (CYP4F12)	807	0
			NP_009184.1	cytochrome P450, subfamily IVF, polypeptide 8; microsomal monooxygenase; flavoprotein-linked monooxygenase	804	0
			NP_076433.1	cytochrome P450 isoform 4F12	803	0
			AAH35350.1	similar to cytochrome P450	802	0
			CAD38795.1	hypothetical protein	794	0
			AAC11543.1	F22329_1	721	0
			XP_029070.2	similar to Cytochrome P450 4F12 (CYP4F12)	687	0
			BAC04868.1	unnamed protein product	655	0
			XP_065069.2	similar to CYTOCHROME P450 4F6 (CYP4F6)	635	0
			XP_065068.1	similar to Cytochrome P450 4F12 (CYP4F12)	620	1E-177
			BAA02145	cytochrome P-450L1BV	590	1E-168
			Q02928	Cytochrome P450 4A11 precursor (CYP1A11) (Fatty acid omega-hydroxylase) (P-450 HK omega) (Lauric acid omega-hydroxylase) (CYP4A11) (P450-HL-omega)	400	1E-111
			NP_000769.1	cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega alkane-1 monooxygenase; lauric acid omega-hydroxylase	397	1E-110
			I65981	fatty acid omega-hydroxylase (EC 1.14.15.-) cytochrome P450 4A11 -	390	1E-108
NM_007899	Mm.4433	F.2.18 (5011)	AAH23505.1	Similar to extracellular matrix protein 1	697	0
NP_031925.1			NP_004416.1	extracellular matrix protein 1, isoform 1 precursor, secretory component p85	697	0

202

NP_057913.1				A34372	complement C6 precursor [validated]			1246	0
				XP_170508.1	similar to Complement component C6 precursor			916	0
				AAB59433.1	complement component C6			760	0
				NP_000578.1	complement component 7 precursor			397	1E-110
				CAA60121.1	complement C7			394	1E-109
NM_021525	Mm28630	F:2.19 (7to19)		AAH01025.1	Similar to RNA cyclase homolog			729	0
NP_067500.1				Q9Y2F8	RNA 3'-terminal phosphate cyclase-like protein			727	0
				NP_005763.2	RNA cyclase homolog			724	0
				AAI29016.1	HSPC338			637	0
				AAD32456.1	RNA cyclase homolog			514	1E-146
NM_022434	Mm.10976	F:2.19 (5to19)		AAC08589.1	cytochrome P-450			855	0
NP_071879.1				BAA75823.1	Leukotriene B4 omega-hydroxylase			855	0
				NP_001073.3	cytochrome P450, subfamily IVF, polypeptide 2; leukotriene B4 omega-hydroxylase; leukotriene B4 20-			853	0
				Q9HB16	Q9HB16 *			848	0
				NP_067010.1	cytochrome P450, subfamily IVF, polypeptide 11			848	0
				AAC50052.2	cytochrome P450 4F2			845	0

5

10

15

20

201

				erythroblastic leukemia viral oncogene homolog 2 (neuro/glioblastoma derived oncogene homolog)		
				AAH02706.1	292	2E-78
				Similar to v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3		
				AAD56009.2	283	9E-76
				herstatin		
20	NM_021522	Mm.25149	F:2.21 (5to19)	NP_003142.1		
	NP_067497.1				910	0
	NM_007711	Mm.28842	F:2.2 (YtoM)	AAB95161		
25	NP_031737.1			chloride channel protein 3	1420	0
				NP_001820		
				chloride channel 3; CIC-3	1415	0
				P51799		
				Chloride channel protein 3 (CIC-3)	1403	0
				BAC54560		
				clcn3e	1368	0
				P51793		
				Chloride channel protein 4 (CIC-4)	1152	0
30				NP_001821		
				chloride channel 4; CIC-4	1149	0
				NP_000075		
				chloride channel 5; Chloride channel-5	1098	0
				NP_032277		
				chloride channel protein, kidney - human	421	1E-117
	NM_008245	Mm.23896	F:2.2 (7to19)	NP_002720.1		
35	NP_032271.1			hematopoietically expressed homeobox; proline-rich homeodomain-containing transcription factor	381	1E-105
				JN0767		
				homeobox protein HHEX	380	1E-105
				AAH14336.1		
				Similar to hematopoietically expressed homeobox	379	1E-105
				CAA79730.1		
				meobox related protein	246	2E-65
40	A K 0 0 3 1 2 1	Mm.30724	F:2.2 (5to19)	NP_076632.1		
	BAB22581.1			hypothetical protein MGC32719 similar to collectins	420	1E-116
				NP_006429.1		
				collectin sub-family member 10; collectin liver 1; collectin 34	228	2E-58
	NM_016704	Mm.20247	F:2.2 (5to19)	NP_000056.1		
				Complement component 6 precursor	1249	0

200

NM_007912	Mm.8534	F.2.21 (51019)	P00533	Epidermal growth factor receptor precursor (Receptor protein-tyrosine kinase ErbB-1)	1160	0
NP_031938.1			AAAS2371.1	aberrant epidermal growth factor receptor	1160	0
			NP_003219.1	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian); epidermal growth factor receptor (avian erythroblastic leukemia viral (v-erb-b) oncogene homolog); Epidermal growth factor receptor	1157	0
			AAG35786.1	p110 epidermal growth factor receptor	1141	0
			AAG35790.1	truncated epidermal growth factor receptor	1141	0
			CAA25282.1	EGF (1 is 2nd base in codon)	942	0
			1007208A	epidermal growth factor receptor	884	0
			AAC50802.1	epidermal growth factor receptor precursor	700	0
			NP_003226.1	v-erb-a erythroblastic leukemia viral oncogene homolog 4; avian erythroblastic leukemia viral (v-erb-b2) oncogene homolog 4; v-erb-a avian erythroblastic leukemia viral oncogene homolog-like	626	1E-179
			NP_001973.1	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian); Transformation gene ERBB-3; v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3	603	1E-172
			A30223	kinase-related transforming protein (erbB3) (HC 2.1.1.) precursor	602	1E-172
			P21860	Receptor protein-tyrosine kinase erbB-3 precursor (c-erbB3) (Tyrosine kinase-type cell surface receptor HER3)	602	1E-172
			22219397	Chain A, Structure Of The Her3 (ErbB3) Extracellular Domain	602	1E-172
			P04626	Receptor protein-tyrosine kinase erbB-2 precursor (p185erbB2) (NEU/ proto-oncogene) (C-erbB-2) (Tyrosine kinase-type cell surface receptor HER2) (MLN 19)	569	1E-162
			NP_004439.1	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog. Avian erythroblastic leukemia viral (v-erb-b2) oncogene homolog 2; v-erb-b2 avian	569	1E-162

5

10

15

1.99

NM_018754	Mm.2758	F:2.22 (50 <sup>3</sup> )	NP_004133.1	stratifu		471	1E-133
NP_061224.1			S38956	epithelial cell marker protein 1		468	1E-131
			AAH01550.1	Similar to stratifu		397	1E-110
			NP_003397.1	tyrosine 3/tryptophan 5 -monoxygenase activation protein, zeta polypeptide; protein kinase C inhibitor protein-1; phospholipase A2		342	6E-94
			NP_006817.1	tyrosine 3/tryptophan 5 -monoxygenase activation protein, theta polypeptide; 14-3-3 protein tau		341	2E-93
			NP_003395.1	tyrosine 3-monoxygenase/tryptophan 5-monoxygenase activation protein, beta polypeptide; 14-3-3 protein beta/alpha; Protein kinase C inhibitor protein-1; Protein 1054		326	6E-90
			NP_036611.2	tyrosine 3-monoxygenase/tryptophan 5-monoxygenase activation protein, gamma polypeptide		319	7E-87
			NP_003396.1	tyrosine 3/tryptophan 5 -monoxygenase activation protein, eta polypeptide		314	2E-85
			AAA35483.1	14-3-3n		311	1E-84
			S38332	protein 14-3-3 eta chain		307	3E-83
NM_007825	Mm.4781	F:2.22 (50 <sup>19</sup> )	AAC95426.1	oxysterol 7alpha-		640	0
NP_031851.1			NP_004811.1	cytochrome P450, subfamily VIIb, polypeptide 1; oxysterol 7alpha-hydroxylase		640	0
			P22680	Cytochrome P450 7A1 (Cholesterol 7alpha-monoxygenase) (CYPVII) (Cholesterol 7alpha-hydroxylase)		313	5E-85
NM_021354	Mm.41803	F:2.21 (70 <sup>19</sup> )	NP_001379.1	developmentally regulated GTP binding protein 2		653	0
NP_067329.1			AAH00493.1	developmentally regulated GTP-binding protein 2		650	0
			AAH20803.1	developmentally regulated GTP binding protein 1		364	1E-100
			NP_004138.1	developmentally regulated GTP binding protein 1; neural precursor cell expressed, developmentally down-regulated 3; developmentally regulated GTP-binding protein 1		362	1E-100

5

10

15

20

198

			AAI50342.1	brain-muscle-ARNT-like transcription factor 2d	545	1E-153
			AAF71306.1	bHLH-PAS transcription factor MOP9	539	1E-152
			AAF71307.1	bHLH-PAS transcription factor MOP9	538	1E-151
			AAH00172.2	Similar to transcription factor BMAL2	536	1E-151
			BAE01485.1	transcription factor BMAL2	533	1E-150
			IC5407	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1e	478	1E-132
			PC4288	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1d	451	1E-125
			NP_001639.1	aryl hydrocarbon receptor nuclear translocator	328	3E-88
			CAD38953.1	hypothetical protein	323	1E-86
			Q9HBZ2	Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2)	318	3E-85
			AAH36099.1	Unknown (protein for MGC33872)	318	3E-85
			NP_055677.1	aryl-hydrocarbon receptor nuclear translocator 2; KIAA0307 gene product; aryl hydrocarbon receptor nuclear translocator 2	317	8E-85
			AAC03365.1	aryl hydrocarbon receptor nuclear translocator, Aml	235	2E-60
			NP_061879.2	protein associated with PRK1; hypothetical protein, associated with PRK1	395	1E-110
			CAB66553.1	hypothetical protein	389	1E-108
			NP_005998.1	zinc finger protein 216	239	2E-63
			XP_048461.1	Similar to protein associated with PRK1; hypothetical protein; associated with PRK1	191	2E-60
			AAI17528.1	unknown	224	6E-59

5

10

15

20

1.9.7

				NP_000187	hydroxysteroid (11-beta) dehydrogenase 2	215	1E-55
				AAB48544	11 beta-hydroxysteroid dehydrogenase 2	214	1E-55
NM_008180	Mm.7504	F:2.23 (50/19)		NP_000169.1	glutathione synthetase	810	0
NP_032206.1							
NM_007468	Mm.4533	F:2.22 (70/11)		P06727	Apolipoprotein A-IV precursor (Apo-AIV)	432	1E-120
NP_031494.1				CAA31955.1	apolipoprotein A-IV	431	1E-119
				NP_000473.1	apolipoprotein A-IV precursor	428	1E-119
				LPHTA4	apolipoprotein A-IV precursor	426	1E-118
				AAA51748.1	apolipoprotein A-IV precursor	422	1E-117
				AAB59516.1	apolipoprotein A-IV	277	2E-73
NM_007489	Mm.12177	F:2.22 (70/11)		NP_001169.2	aryl hydrocarbon receptor nuclear translocator-like	1219	0
NP_031515.1							
				JCS405	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1b	1218	0
				O00327	BMAL1 protein (Brain and muscle ARNT-like 1) (Member of PAS protein 3) (Basic-helix-loop	1130	0
				AAC51213.1	helix-PAS orphan MOP3) (BHLH-PAS protein JAP3)	1102	0
					PAS protein 3		
				NP_064568.2	transcription factor BMAL2	560	1E-158
				AAL50339.1	brain-muscle-ARNT-like transcription factor 2a	557	1E-157
				AAL50340.1	brain-muscle-ARNT-like transcription factor 2b	551	1E-155
				AAL50341.1	brain-muscle-ARNT-like transcription factor 2c	545	1E-153

5

1.0

15

20



196

AAA35835.1	FGF receptor-1 precursor	257	1E-67
AAA75007.1	basic fibroblast growth factor receptor protein.	257	1E-67
NP_065680.1	ret proto-oncogene isoform b; RET transforming sequence; hydroxyaryl-protein kinase; cadherin family member 12; oncogene RET	253	2E-66
CAA31408.1	ret tyrosine kinase (AA 1 - 860)	253	2E-66
NP_066124.1	ret proto-oncogene isoform a; RET transforming sequence; hydroxyaryl-protein kinase; cadherin family member 12; oncogene RET	253	2E-66
NP_065681.1	ret proto-oncogene isoform c; RET transforming sequence; hydroxyaryl-protein kinase; cadherin family member 12; oncogene RET	253	2E-66
AAH04257.1	ret proto-oncogene (multiple endocrine neoplasia MEN2A, MEN2B and medullary thyroid carcinoma 1, Hirschsprung disease)	252	3E-66
AAA36786.1	tyrosine kinase	251	6E-66
I38153	gene ret11 protein - human	251	6E-66
B34735	protein-tyrosine kinase (EC 2.7.1.12) (ret)	249	4E-65
AAA36524.1	papillary thyroid carcinoma-encoded protein	249	4E-65
JN0290	protein-tyrosine kinase (EC 2.7.1.12) (clone lambda-ret-1)	248	5E-65
JN0291	protein-tyrosine kinase (EC 2.7.1.12) (clone lambda-ret-5)	248	5E-65
CAB46483.1	RET tyrosine kinase receptor	248	6E-65
A4A60266.1	RET tyrosine kinase/cAMP protein kinase A subunit RI	247	1E-64
A39061	protein-tyrosine kinase (EC 2.7.1.12) FLT3 (fms homolog)	224	1E-57
ITFGKA	Chian A, Crystal Structure Of The Tyrosine Kinase Domain Of Fibroblast Growth Factor Receptor 1	223	2E-57
NP_075599.1	fibroblast growth factor receptor 1 isoform 9 precursor; fms-related tyrosine kinase-2; heparin-binding growth factor receptor; FMS-like tyrosine kinase 2; basic fibroblast growth factor receptor 1; N-sun tyrosine kinase; FLG protein; protein-tyrosine kinase; tyrosylprotein kinase; hydroxyaryl-protein kinase	216	2E-55
Mm.8877	hydroxysteroid (17-beta) dehydrogenase 2	391	1E-109
NP_03216.1	11beta-hydroxysteroid dehydrogenase (EC 1.1.1.146) type 2	215	8E-56
AAH36780	hydroxysteroid (11-beta) dehydrogenase 2	215	8E-56

5

10

15

20

195

AAA58470.1	growth factor receptor	270	2E-71
NP_000133.1	fibroblast growth factor receptor 3, isoform 1 precursor; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase; human tyrosine kinase JTK4	270	2E-71
AA022078.1	fibroblast growth factor receptor 3	270	2E-71
NP_075254.1	fibroblast growth factor receptor 3, isoform 2 precursor; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase; human tyrosine kinase JTK4	270	2E-71
IGLOA	Chain A, The Fgf2 Tyrosine Kinase Domain	269	3E-71
AAH15035.1	similar to fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	258	5E-68
AAA33837.1	fibroblast growth factor receptor (FGFR) transmembrane form	257	1E-67
NP_075594.1	fibroblast growth factor receptor 1 isoform 4 precursor; fms-related tyrosine kinase-2; heparin-binding growth factor receptor; FMS-like tyrosine kinase 2; basic fibroblast growth factor receptor 1; N-sam tyrosine kinase; FLG protein; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase	257	1E-67
NP_075593.1	fibroblast growth factor receptor 1 isoform 3 precursor; fms-related tyrosine kinase-2; heparin-binding growth factor receptor; FMS-like tyrosine kinase 2; basic fibroblast growth factor receptor 1; N-sam tyrosine kinase; FLG protein; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase	257	1E-67
CAA68679.1	tyrosine kinase	257	1E-67
CAA36101.1	precursor polypeptide (AA-21 to 801)	257	1E-67
NP_000595.1	fibroblast growth factor receptor 1 isoform 1 precursor; fms-related tyrosine kinase-2; heparin-binding growth factor receptor; FMS-like tyrosine kinase 2; basic fibroblast growth factor receptor 1; N-sam tyrosine kinase; FLG protein; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase	257	1E-67
AAA35938.1	heparin-binding growth factor receptor	257	1E-67
NP_056934.2	fibroblast growth factor receptor 1 isoform 2 precursor; fms-related tyrosine kinase-2; heparin-binding growth factor receptor; FMS-like tyrosine kinase 2; basic fibroblast growth factor receptor 1; N-sam tyrosine kinase; FLG protein; protein-tyrosine kinase; tyrosyl/protein kinase; hydroxyl-tyrosine kinase	257	1E-67
AAH18128.1	similar to fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	257	1E-67

5

10

15

194

NP_000132.1	fibroblast growth factor receptor 2 isoform 1 precursor, keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase; fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-aryl-protein kinase	281	5E-75
AAK94205.1	keratinocyte growth factor receptor 2 isoform BEK	281	7E-75
AAK94209.1	keratinocyte growth factor receptor 2 isoform K-sam-1IC2	281	7E-75
AAH39243.1	Similar to fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor; craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	281	7E-75
BAA89299.1	K-sam-101	281	9E-75
BAA89301.1	K-sam-103	281	9E-75
BAA89296.1	K-sam-1IH1	281	9E-75
BAA89298.1	K-sam-1IH3	281	9E-75
AAD31560.1	Fibroblast growth receptor 2 Ig1Ib isoform	280	1E-74
NP_075262.1	fibroblast growth factor receptor 2 isoform 6 precursor, keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase; fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-aryl-protein kinase	280	1E-74
A35969	heparin-binding growth factor receptor; K-sam precursor	280	1E-74
NP_075417.1	Fibroblast growth factor receptor 2 isoform 10 precursor, keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase; fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-aryl-protein kinase	280	2E-74
AAK94208.1	keratinocyte growth factor receptor 2 isoform K-sam-1IC3	280	2E-74
NP_075261.1	fibroblast growth factor receptor 2 isoform 5 precursor, keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase; fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-aryl-protein kinase	278	7E-74
AAD31561.1	fibroblast growth factor receptor 2 isoform Ig1Ic isoform	272	4E-72
BAC45037.1	isoform of FGFR2	272	4E-72
NP_075259.1	fibroblast growth factor receptor 2 isoform 3 precursor, keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase; fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-aryl-protein kinase	270	2E-71

5

10

15

193

		NP_002444.1	kinase insert domain receptor (a type III receptor tyrosine kinase); Kinase insert domain receptor	326	2E-88
		NP_002011.1	ins-related tyrosine kinase 4, ins-related tyrosine kinase-4 (vascular endothelial growth factor receptor 3)	325	3E-88
		CAA43837.1	membrane protein	323	1E-87
		IC1402	protein-tyrosine kinase (EC 2.7.1.112) KDR - human	323	1E-87
		CAD77356.1	KIT protein	313	1E-84
		IVR2A	Chain A, Human Vascular Endothelial Growth Factor Receptor 2 (Kdr) Kinase Domain	286	3E-76
		NP_075258.1	fibroblast growth factor receptor 2 isoform 2 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	284	8E-76
		NP_075264.2	fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		
			fibroblast growth factor receptor 2 isoform 8 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	284	1E-75
		NP_075419.1	fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		
			fibroblast growth factor receptor 2 isoform 12 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	284	1E-75
		A41794	fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		
		AAK94206.1	keratinocyte growth factor receptor 2 isoform KGFPR	284	1E-75
		NP_075420.1	fibroblast growth factor receptor 2 isoform 13 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	283	1E-75
		BAA89300.1	fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		
			K-sam-II02	283	2E-75
		NP_075263.1	fibroblast growth factor receptor 2 isoform 7 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	283	2E-75
		Q01742	fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		
		BAA89297.1	fibroblast growth factor receptor BFR-2 precursor.	283	2E-75
		NP_075418.1	K-sam-III2	281	5E-75
			fibroblast growth factor receptor 2 isoform 11 precursor; keratinocyte growth factor receptor; K-sam protein; protein tyrosine kinase, receptor like 14; FGF receptor; bacteria-expressed kinase;	281	5E-75
			fibroblast growth factor receptor BEK; tyrosylprotein kinase; hydroxyl-tyrosine kinase		

5

10

15

192

NM_011656	Mm.10214	F:2.24 (11o19)	NP_064512.1	tufelin 1	681	0
NP_035786.1			AAH02933.1	Similar to tufelin 1	622	1E-178
			BAB15615.1	unnamed protein product	271	3E-72
NM_021099	Mm.4394	F:2.23 (YoO)	AAC50969.1	KIT protein	1532	0
NP_066922.1			NP_000213.1	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog precursor	1526	0
			CAA27300.1	put. c-fms precursor	647	0
			NP_005202.2	colony stimulating factor 1 receptor precursor; FMS proto-oncogene; CD115 antigen; macrophage colony stimulating factor 1 receptor; similar to mouse Friend murine leukemia virus integration site 2	647	0
			AAH47521.1	colony stimulating factor 1 receptor, formerly McDonough feline sarcoma viral (v-fms) oncogene homolog	645	0
			NP_006197.1	platelet-derived growth factor receptor alpha precursor	511	1E-144
			AAA36427.1	platelet-derived growth factor receptor	484	1E-136
			NP_007600.1	platelet-derived growth factor receptor beta precursor; beta platelet-derived growth factor receptor	484	1E-136
			AAH32224.1	platelet-derived growth factor receptor, beta polypeptide	483	1E-135
			CAA81393.1	FLT3 receptor tyrosine kinase	442	1E-123
			NP_004110.1	fms-related tyrosine kinase 3	439	1E-122
			A36873	protein-tyrosine kinase [BC 2.7.1.12] STK-1 precursor	431	1E-120
			NP_002010.1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	358	5E-98
			AAO16449.1	vascular endothelial growth factor receptor	357	7E-98
			P35916	Vascular endothelial growth factor receptor 3 precursor (VEGFR-3)(Tyrosine-protein kinase receptor FLT4)	327	8E-89
			CAA48290.1	FLT4	327	8E-89
			AAO16450.1	vascular endothelial growth factor receptor 2	326	2E-88

5

10

15

20

191

NM_013585	Mm.16251	F:2.25 (Sto19)	S27332	proteasome endopeptidase complex (EC 3.4.25.1)	272	5E-73
NP_038613.1			NP_002791.1	proteasome beta 9 subunit isoform 1 proprotein; proteasome subunit, beta type, 9; proteasome-related gene 2; proteasome chain 7; macropain chain 7; low molecular mass protein 2; multicatalytic endopeptidase complex chain 7; proteasome catalytic subunit 1i; proteasome subunit beta 6i	269	4E-72
			NP_683756.1	proteasome beta 9 subunit isoform 2 proprotein; proteasome subunit, beta type, 9; proteasome-related gene 2; proteasome chain 7; macropain chain 7; low molecular mass protein 2; multicatalytic endopeptidase complex chain 7; proteasome catalytic subunit 1i; proteasome subunit beta 6i	256	3E-68
NM_008035	Mm.2724	F:2.24 (YtoO)	CAA49267.1	folate receptor	421	1E-116
NP_032061.1			NP_000794.1	folate receptor 2 precursor	419	1E-116
			AAA17370.1	folate binding protein	419	1E-116
			NP_000795.1	folate receptor 3 precursor	400	1E-110
			NP_000793.1	folate receptor 1 (adult)	374	1E-102
			AAA74896.1	folate-binding protein	308	1E-100
			XP_169247.1	similar to Folate receptor gamma precursor (FR-gamma) (Folate receptor 3)	313	4E-84
			AAAB1937.1	folate binding protein	164	4E-74
NM_025649	Mm.2787	F:2.24 (YtoO)	NP_055443	gene predicted from cDNA with a complete coding sequence; caught by MAD Two 2	424	1E-117
NP_079925.1						

5

10

15

190

NM_059112.1				interleukin 1 receptor accessory protein-like 2; interleukin 1 receptor 9; IL-1 receptor; X-linked interleukin-1 receptor accessory protein-like 2; IL-1 receptor accessory protein-like 2	206	3E-51
AAFS9412.1				X-linked interleukin-1 receptor accessory protein-like 2	206	3E-51
NM_008295	Mm.17910	F:2.25 (YtoO)		hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1; Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid	528	1E-149
NP_032321.1				3-beta-hydroxysteroid dehydrogenase/delta-5-delta-4-isomerase	526	1E-149
AAA51831				hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2; Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid	513	1E-145
NP_000189				steroid dehydrogenase, 3 beta- and steroid		
AAA30001				3-beta-hydroxysteroid dehydrogenase gene	481	1E-136
CAC19801				dJ871G17.4 (novel 3-beta hydroxysteroid dehydrogenase/isomerase family member)	360	3E-99
AAAM08704				3-beta-hydroxysteroid dehydrogenase	353	5E-97
XP_060827				similar to 3-beta-hydroxysteroid dehydrogenase	258	2E-68
AA037824				3 beta-hydroxy-delta 5-C27-steroid oxidoreductase	225	2E-58
NP_079469				3 beta-hydroxy-delta 5-C27-steroid oxidoreductase	223	8E-58
CAC19803				dJ871G17.6 (novel 3-beta hydroxysteroid dehydrogenase/isomerase family member)	202	8E-52
AA014414				3 beta-hydroxysteroid dehydrogenase homolog pseudogene	199	7E-51
NM_004961.1				insulin-like growth factor binding protein, acid labile subunit; INSULIN-LIKE GROWTH	805	0
NP_032366.1	Mm.3135	F:2.25 (7to19)		FACTOR BINDING PROTEIN COMPLEX ACID LABILE CHAIN PRECURSOR		
AAH25681.1				insulin-like growth factor binding protein, acid labile subunit	804	0
NM_008343	Mm.29254	F:2.25 (5to11)		insulin-like growth factor binding protein 3	442	1E-123
NP_032369.1						
NP_000590.1				insulin-like growth factor binding protein 5	206	4E-52
NM_008929	Mm.12616	F:2.25 (5to19)		interferon-induced double-stranded RNA-activated protein kinase inhibitor	897	0
NP_032955.1						
AAH33823.1				Similar to DnaJ (Hsp40) homolog, subfamily C, member 3	213	8E-55

5

10

15

20

25

189

5	NM_028740	Mm.159128	F:2.27 (5o19)	alpha-1-antichymotrypsin precursor	206	4E-53
	NP_083016.1			alpha-1-antichymotrypsin	206	4E-53
				Chain A, Alpha 1-Antichymotrypsin Serpin In The Delta Conformation (Partial Loop Insertion)	206	4E-53
				serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin, antitrypsin), member 3	206	4E-53
				XP_028322.1 similar to Alpha-1-antichymotrypsin precursor (ACT)	206	4E-53
10				alpha 1 antichymotrypsin	206	4E-53
				alpha-1-antichymotrypsin precursor	206	4E-53
				NP_001076.1 alpha-1-antichymotrypsin, precursor, alpha-1-antichymotrypsin, antichymotrypsin	202	6E-52
				ITHUC alpha-1-antichymotrypsin precursor	202	6E-52
				I313184C chymotrypsin inhibitor	202	6E-52
15	NM_016875	Mm.29286	F:2.26 (YuoO)	germ cell specific Y-box binding protein, conitin	285	1E-76
	NP_058571.1			germ cell specific Y-box binding protein	285	1E-76
				interleukin 1 receptor, type I precursor, interleukin 1 receptor alpha, type I, interleukin receptor	823	0
				I, antigen CD121a		
20	NM_008362	Mm.896	F:2.26 (5o19)	Interleukin-1 Receptor With The Interleukin-1 Receptor Antagonist (IL1Ra)	451	1E-125
	NP_032388.1			Type-1 Interleukin-1 Receptor Complexed With Interleukin-1 Beta	448	1E-124
				IL-1 Receptor Type 1 Complexed With Antagonist Peptide Afl0847	445	1E-123
				XP_002685.3 similar to IL-1Rrp2	356	2E-96
				AAG21368.1 IL-1Rrp2	356	2E-96
25				interleukin 1 receptor-like 2	354	7E-96
				interleukin 1 receptor-like 1, interleukin 1 receptor 1, ST2V protein	208	5E-52
				NP_057316.2 interleukin 1 receptor-like 1, interleukin 1 receptor 1, ST2V protein		



188

				Q9P255	Hypothetical zinc finger protein KIAA1473	313	9E-85
				BAB85542.1	KIAA1956 protein	313	9E-85
				XP_085836.1	similar to Hypothetical zinc finger protein KIAA1956	313	9E-85
				XP_047550.1	similar to Hypothetical zinc finger protein KIAA1473	313	9E-85
				NP_003406.1	zinc finger protein 268	312	1E-84
				AAH36038.1	Unknown (protein for MGC33240)	312	1E-84
				AAK69307.1	ZNF768B	312	1E-84
				S47071	finger protein HZF3, Kneippel-related - human (fragment)	312	2E-84
				NP_037512.1	zinc finger protein 228	312	2E-84
NM_007517	Mm.2146	P:2.27 (7to19)		AAD43017.1	ancient ubiquitous 46 kDa protein AUP1	549	1E-155
NP_031543.1				AAD43010.1	AUP1 homolog	548	1E-155
				BAB14753.1	unnamed protein product	492	1E-139
				NP_036235.1	ancient ubiquitous protein 1	431	1E-119
NM_018816	Mm.2161	P:2.27 (5to19)		XP_165719.1	similar to Apolipoprotein M (ApoM) (G3a) (HSPC336)	319	3E-87
NP_061286.1				CAB51604.1	G3a protein	299	2E-81
				AAF29014.1	HSPC336	262	4E-70

5

10

15

20

1.87

			NP_003442.1 zinc finger protein 177	317	5E-86
			XP_087503.1 similar to zinc finger protein 91 (HPF7, HTF10)	317	5E-86
			XP_033888.3 similar to Zinc finger protein 41	317	6E-86
			CAC88162.1 bB479F17.3 (zinc finger protein 41)	317	6E-86
			NP_700359.1 zinc finger protein 41	317	6E-86
			A54661 zinc finger protein ZNF41 - human	317	6E-86
			AAH22992.1 Unknown (protein for MGC:29879)	317	6E-86
			XP_166367.1 similar to Zinc finger protein 184	317	6E-86
			BAC04216.1 unnamed protein product	316	8E-86
			NP_065704.1 zinc finger protein 287	316	8E-86
			NP_061025.3 zinc finger protein 331; zinc finger protein 463; C2H2-like zinc finger protein	315	1E-85
			AAF78075.1 KRAB zinc finger protein	315	1E-85
			AAH36714.1 Unknown (protein for IMAGE:4846514)	315	2E-85
			T12489 hypothetical protein DKFZp572P0920.1 - human	315	2E-85
			XP_032810.1 similar to Zinc finger protein 20 (Zinc finger protein KOX13) (DKFZp572P0920)	315	2E-85
			AAF88107.1 Hypothetical zinc finger-like protein	315	2E-85
			NP_612203.1 TRAF6-inhibitory zinc finger protein; TRAF6-binding zinc finger protein	314	3E-85
			XP_092088.3 similar to zinc finger protein 91 (HPF7, HTF10)	314	3E-85
			XP_047554.4 similar to Hypothetical zinc finger protein KIAA1473	314	4E-85
			NP_006620.1 zinc finger protein 271	313	5E-85

5

1.0

1.5

2.0

186

		XP_092090.2	similar to Hypothetical zinc finger protein KIAA1473	320	6E-87
		BAA24050.1	Zinc-finger protein	320	6E-87
		NP_443092.1	Kruppel-like zinc finger protein	319	1E-86
		XP_171940.1	similar to BC37295_1	318	2E-86
		NP_653294.1	hypothetical protein FLJ30932	318	2E-86
		XP_064929.5	similar to Zinc finger protein 20 (Zinc finger protein KOX13)	318	2E-86
		NP_079009.1	hypothetical protein FLJ14345	318	2E-86
		NP_003416.1	zinc finger protein 45 (a Kruppel-associated box (KRAB) domain polypeptide); Zinc finger protein-45 (a Kruppel-associated box (KRAB) domain	318	2E-86
		AAF63030.1	Zinc finger protein ZNF45	318	2E-86
		NP_008889.1	zinc finger protein 16 (KOX 9)	318	2E-86
		CAD39111.1	hypothetical protein	318	2E-86
		XP_092093.1	similar to Zinc finger protein 85 (Zinc finger protein HPF4) (HTF1)	318	2E-86
		P17020	Zinc finger protein 16 (Zinc finger protein KOX9)	318	2E-86
		AAH06528.1	zinc finger protein 43 (HTF6)	318	3E-86
		XP_086128.1	similar to Zinc finger protein 35 (Zfp-35)	318	3E-86
		XP_065116.3	similar to zinc finger protein 91 (HPF7, HTF10)	317	4E-86
		NP_003414.1	zinc finger protein 43 (HTF6) [	317	4E-86
		AAH35579.1	Similar to zinc finger protein 208	317	4E-86
		NP_061121.1	zinc finger protein ZFP	317	5E-86

185

		XP_091983.1 similar to Zinc finger protein 135	324	4E-88
		CAB94232.2 zinc finger protein	323	5E-88
		NP_003419.1 zinc finger protein 84 (HPT2)	323	5E-88
		B32891 finger protein 2, placental	323	5E-88
		NP_055295.1 zinc finger protein AF020591	323	7E-88
		AAC51180.1 kruppel-related zinc finger protein	323	9E-88
		XP_092097.1 similar to Zinc finger protein 93 (Zinc finger protein H1F34)	322	1E-87
		AAH36110.1 Similar to zinc finger protein 208	322	1E-87
		BAC04610.1 unnamed protein product	322	2E-87
		NP_612143.1 hypothetical protein FLJ1526	322	2E-87
		NP_067039.1 zinc finger protein 71; endothelial zinc finger protein induced by tumor necrosis factor alpha	321	3E-87
		NP_003399.1 zinc finger protein 37 homolog (mouse); Zinc finger protein-37, mouse, homolog of; zinc finger protein homologous to Zfp37 in mouse	321	3E-87
		BAC04064.1 unnamed protein product	321	3E-87
		Q9Y6Q3 Zinc finger protein ZFP-37	321	3E-87
		AAD23608.1 BC37295_2 (partial)	321	3E-87
		AAL58442.1 zinc finger protein 328	321	3E-87
		BAB47481.1 KIAA1852 protein	321	3E-87
		AAH37209.1 Unknown (protein for MGC-41956)	320	4E-87
		XP_171752.1 similar to zinc finger protein 29	320	4E-87

5

10

15

184

				XP_031283.1	similar to Hypothetical zinc finger protein KIAA1710	337	3E-92
				P35789	Zinc finger protein 93 (Zinc finger protein HTF34)	336	8E-92
				NP_003427.1	zinc finger protein 135 (clone pHZ-17)	336	1E-91
				NP_653290.2	hypothetical protein FLJ32191	335	1E-91
				BAB71257.1	unnamed protein product	333	8E-91
				BAC04764.1	unnamed protein product	332	2E-90
				NP_003420.1	zinc finger protein 85 (HPF4, HTF1)	330	5E-90
				BAA86512.1	KIAA1198 protein	328	3E-89
				XP_032674.1	similar to Hypothetical zinc finger protein KIAA1198	328	3E-89
				NP_660338.1	similar to Zinc finger protein 136	327	4E-89
				BAB71272.1	unnamed protein product	327	6E-89
				XP_063387.2	similar to Zinc finger protein 135	326	1E-88
				XP_086070.1	similar to Zinc finger protein 93 (Zinc finger protein HTF34)	325	1E-88
				NP_003421.1	zinc finger protein 91 (HPF7, HTF10)	325	1E-88
				XP_068538.2	similar to Zinc finger protein 93 (Zinc finger protein HTF34)	325	2E-88
				XP_028314.1	similar to KRAB zinc finger protein KR18	324	3E-88
				XP_115638.2	similar to Zinc finger protein 208	324	3E-88
				TI14757	hypothetical protein DKFp572C163.1	324	3E-88

20

25

30

35

183

			NP_003992.2	Fc fragment of IgG, low affinity Iib, receptor for (CD32); Fc fragment of IgG, low affinity II, receptor for (CD32)	296	4E-80
			FL0119	Fc gamma (IgG) receptor Iib precursor	296	4E-80
NM_029813	Mm.159813		NP_689814.1	hypothetical protein FLJ38281	373	1E-103
NP_084089.1			XP_091960.1	similar to zinc finger protein 14 (KOX 6); GIOT-4 for gonadotropin inducible transcription repressor-4	373	1E-103
			NP_066358.1	zinc finger protein 14 (KOX 6); GIOT-4 for gonadotropin inducible transcription repressor-4	364	1E-100
			NP_699189.1	hypothetical protein FLJ90396	364	1E-100
			XP_091958.1	similar to zinc finger protein 14 (KOX 6); GIOT-4 for gonadotropin inducible transcription repressor-4	364	1E-100
			XP_091968.4	similar to zinc finger protein 91 (HPF7, HTF10)	353	6E-97
			AAAF1790.1	ZNF180	347	6E-95
			NP_037388.1	zinc finger protein 180 (HHZ168)	347	6E-95
			NP_003428.1	zinc finger protein 136 (clone pHZ-20)	345	1E-94
			NP_689815.1	hypothetical protein FLJ40981	344	3E-94
			NP_085116.1	hypothetical protein FLJ21628	343	8E-94
			AAD23607.1	BC37295_1	341	2E-93
			BAC04309.1	unnamed protein product	338	2E-92
			BAR21801.1	KIAA1710 protein	337	3E-92
			XP_032812.1	similar to hypothetical protein FLJ40981	337	3E-92

5

10

15

182

			P07864	L-lactate dehydrogenase C chain (LDH-C) (LDH testis subunit) (LDH-X)	494	1E-139
			pdhl10Z	Chain A, Human Heart L-Lactate Dehydrogenase H Chain, Ternary Complex With Nucleo And Oxamate	493	1E-139
			NP_149972.1	lactate dehydrogenase A-like	490	1E-138
			BAB71710.1	unnamed protein product	488	1E-137
			AAA59508.1	lactate dehydrogenase-C	437	1E-122
			XP_062669.6	similar to lactate dehydrogenase A-like	386	1E-107
			NP_659409.1	hypothetical protein MGC23940	343	3E-94
			AAD00638.1	Fc-gamma-RIIb2	309	6E-84
			AAD00641.1	Fc-gamma-RIIb2	306	6E-63
			CAA35713.1	precursor polypeptide (AA -42 to 249)	305	8E-83
			AAA35842.1	IgG Fc fragment receptor precursor	304	2E-82
			AAA36051.1	IgG Fc receptor beta-Fc-gamma-RII	301	1E-81
			CAA35644.1	IgG Fc receptor	301	2E-81
			AAD00639.1	Fc-gamma-RIIb1	301	2E-81
			AAD00637.1	Fc-gamma-RIIb1	301	2E-81
			AAD00640.1	Fc-gamma-RIIb1	297	2E-80
			P21994	Low affinity immunoglobulin gamma FC region receptor II-B precursor (FC-gamma RII-B) (FCRII-B) (IGG FC receptor II-B) (FC-gamma-RIIB) (CD32) (CDW32)	297	3E-80

5

10

15

181

			NP_004963.1	Janus kinase 2; tyrosine-protein kinase JAK2		720	0
			AAD22741.1	JAK3_HUMAN; JANUS KINASE 3; JAK-3; LEUKOCYTE JANUS KINASE; L-JAK		664	0
			AAC50950.1	JAK3		660	0
			NP_000206.1	Janus kinase 3; L-JAK		655	0
			AAC50261	JAK3B		645	0
			AAH28068.1	Similar to Janus Kinase 3 (a protein tyrosine kinase, leukocyte)		243	1E-63
			NP_005527.1	inositol(myo)-1(or 4)-monophosphatase 1		489	1E-138
			ptbpl2/HIM	Inositol-1-(or 4)-monophosphatase (IMPase) (inositol monophosphatase) (Lithium-sensitive myo-inositol monophosphatase A1)		488	1E-138
			NP_055029.1	inositol(myo)-1(or 4)-monophosphatase 2		525	4E-59
			XP_095533.1	similar to Myo-inositol-1(or 4)-monophosphatase (IMPase) (IMP) (inositol monophosphatase) (Lithium-sensitive myo-inositol monophosphatase A1)		322	4E-88
			AAF07824.1	brain myo-inositol monophosphatase A2b, IMPase A2b		301	1E-61
			NP_005557.1	lactate dehydrogenase A		597	1E-170
			ptbll110	Chain A, Human Muscle L-Lactate Dehydrogenase M Chain, Ternary Complex With Nucleic Acid Oxamate		595	1E-170
			NP_002291.1	lactate dehydrogenase B		495	1E-140
			AAA59507.1	lactate dehydrogenase (E.C. 1.1.1.27)		495	1E-140
			NP_002292.1	lactate dehydrogenase C		494	1E-139

5

10

15

20



1.80

			XP_035037.2	similar to MEGF7		200	2E-50
A K 0 5 0 4 9	Mm.158752	F.2.3 (5to19)	AAH31569.1	Similar to RIKEN cDNA 1300018K11 gene		668	0
BAB23775.1			P22792	Carboxypeptidase N 83 kDa chain (Carboxypeptidase N regulatory subunit)		490	1E-137
A K 0 9 8 8 1	Mm.154570	F.2.3 (5to19)	NP_006808.1	endoplasmic reticulum protein 29 precursor; endoplasmic reticulum luminal protein ERp28		430	1E-119
BAB26559.1							
N M _ 0 0 9 5 4 7	Mm.29434	F.2.29 (5to7)	NP_003400.2	zinc finger protein 161 homolog; zinc finger protein homologous to Zfp161 in mouse		839	0
NP_033573.1			O43829	Zinc finger protein Zfp-161 (Zinc finger protein 5) (hZF5)		838	0
			XP_008796.5	similar to zinc finger protein 161 homolog (mouse); zinc finger protein homologous to Zfp161		288	2E-77
				in mouse			
N M _ 0 1 8 7 9 3	Mm.20249	F.2.29 (5to19)	XP_008893.4	similar to Non-receptor tyrosine-protein kinase TYK2		1854	0
NP_061263.1			AAH14243.1	Unknown (protein for MGC20776)		1853	0
			NP_003322.1	tyrosine kinase 2		1839	0
			AAB22747.1	IFN- $\gamma$ , $\gamma$ 2-interferon alpha/beta signaling pathway-related protein tyrosine kinase [human, 1442		1442	0
			A39577	Daudi cell line, Peptide Partial, 899 aa]		924	0
			NP_002218.1	protein-tyrosine kinase (EC 2.7.1.12) JAK1		924	0
				Janus kinase 1			
			AAC23463.1	Jak2 Kinase		720	0
			JW0091	Janus kinase (EC 2.7.-.2) -		720	0

5

10

15

20

179

			BAA09435.1	phakoglobin	279	1E-73
NM_010501	Mm.951					
NP_034631.1		F:2.3 (V%M)	XP_048183.1	similar to Interferon-induced protein with tetratricopeptide repeats 4 (IFTI-4) (Interferon-induced 60 kDa protein) (IFI-60K) (ISG-60) (CTG49) (Retinoic acid-induced gene G protein) (RIG-G)	504	1E-142
			AAH04977.1	interferon-induced protein with tetratricopeptide repeats 4	504	1E-142
			NP_001540.1	interferon-induced protein with tetratricopeptide repeats 4	500	1E-141
			XP_084477.1	similar to Interferon-induced protein with tetratricopeptide repeats 2 (IFTI-2) (Interferon-induced 54 kDa protein) (IFI-54K) (ISG-54 K)	365	1E-101
			AAH32839.1	Similar to interferon-induced protein with tetratricopeptide repeats 2	333	1E-91
			AAH07091.1	Unknown (protein for MGC:14710)	285	1E-76
			NP_001539.1	interferon-induced protein with tetratricopeptide repeats 1; Interferon, alpha-inducible protein (MW 56kD); interferon-induced protein 56	284	2E-76
			NP_036552.1	retinoic acid- and interferon-inducible protein (58kD)	279	8E-75
NM_010917	Mm.4691	F:2.3 (5to11)	MMHUND	nidogen precursor	2165	0
NP_035047.1			NP_002499.1	nidogen (enactin); Nidogen; nidogen (entactin)	2161	0
			CAA37709.1	nidogen	2140	0
			AAAS7261.1	nidogen	1138	0
			NP_031387.1	nidogen 2 (osteonidogen); nidogen 2	788	0
			Q1412	Nidogen-2 precursor (NID-2) (Osteonidogen).	787	0
			XP_051712.2	similar to Nidogen-2 precursor (NID-2) (Osteonidogen)	785	0
			AAH35603.1	Similar to nidogen 2 (osteonidogen)	711	0

5

10

15

20

213

NM_025774	Mm.31643	F:2.13 (5to11)	NP_078929.1	hypothetical protein FLJ13902	209	4E-54
NP_080050.1			AAH14298.1	hypothetical protein FLJ13902	206	5E-53
NM_015775	Mm.24242	F:2.13 (5to19)	NP_001863.1	plasma carboxypeptidase B2 isoform a preproprotein; thrombin-activatable fibrinolysis inhibitor; thrombin-activatable fibrinolysis inhibitor; carboxypeptidase U; carboxypeptidase B-like protein; procarboxypeptidase U; procarboxypeptidase R; plasma procarboxypeptidase B	733	0
NP_062749.1						
			AAH07057.1	carboxypeptidase B2 (plasma)	733	0
			NP_057497.2	plasma carboxypeptidase B2 isoform b; thrombin-activatable fibrinolysis inhibitor; thrombin-activatable fibrinolysis inhibitor; carboxypeptidase U; carboxypeptidase B-like protein; procarboxypeptidase U; procarboxypeptidase R; plasma procarboxypeptidase B	587	1E-167
			BAA90475.1	carboxypeptidase B-like protein	585	1E-167
			CAA12163.1	procarboxypeptidase B	360	4E-99
			P15086	Carboxypeptidase B precursor (Pancreas-specific protein) (PASP)	359	6E-99
NM_008348	Mm.26658	F:2.12 (YtoO)	NP_001549	interleukin 10 receptor, alpha precursor	578	1E-164
NP_032374.1			IJTVR	Chain R, Human IL-10 IL-10R1 Complex	237	7E-62
NM_020590	Mm.14638	F:2.12 (7to19)	NP_113600.1	GABA(A) receptor-associated protein like 1; early estrogen-regulated protein	245	9E-66
NP_065615.1						
			NP_115957.1	GABA(A) receptors associated protein like 3	226	3E-60

## 214

			Chain A, Solution Structure Of Human Gaba Receptor Associated Protein Gabarap	216	6E-57
			GABA(A) receptor-associated protein; GABA(A)-receptor-associated protein	216	6E-57
NM_011375	Mm.38748	F:2.12 (5019)	sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase); ganglioside G(M3) Synthase	628	1E-179
NP_035505.1			CMP-NeuAc:lactosylceramide alpha-2,3-	626	1E-178
			sialyltransferase 6 isoform j; Gal beta-1,3(4)GlcNAc alpha-2,3 sialyltransferase; CMP-N-	213	1E-53
			acetylneuraminic-beta-1,4-galactoside alpha-2,3-sialyltransferase; alpha-2,3-sialyltransferase II; alpha 2,3-sialyltransferase III		
			Gal beta 1,3(4) GlcNAc alpha 2,3 sialyltransferase	202	2E-50
NM_013563	Mm.2923	F:2.11 (YtoO)	interleukin 2 receptor, gamma chain, precursor; Interleukin-2 receptor, gamma; common cytokine	488	1E-138
NP_038591.1			receptor gamma chain; CD132		
NM_021791	Mm.45874	F:2.11 (YtoM)	solute carrier family 7 (cationic amino acid transporter, y+ system), member 9; solute carrier	754	0
NP_067266.1			family 7, member 9; solute carrier family 7 (cationic amino acid, transporter, y+ system), member		
			9		
			glycoprotein-associated amino acid transporter, h50,4AT1	751	0
			solute carrier family 7 (cationic amino acid transporter, y+ system), member 5; Membrane protein	347	3E-95
			El6; Solute carrier family 7, member 5; 4F2 light chain		
			amino acid transporter El6	347	3E-95
			sodium-independent neutral amino acid transporter LAT1	346	7E-95
			Similar to solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	346	7E-95
			4F2 light chain	346	7E-95
			unpaired protein product	345	2E-94
			Y+L amino acid transporter 1 (y(+)-type amino acid transporter 1) (y+LAT1) (Y+LAT1)	345	2E-94
			(Monocyte amino acid permease 2) (MOP-2)		
			solute carrier family 7, (cationic amino acid transporter, y+ system) member 11; cystine/glutamate	344	2E-94
			transporter		

215

			NP_003973	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 7	343	3E-94
			NP_003974	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 6	337	3E-92
			Q9JH15	Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2),	328	2E-89
			BAB40574	cystine/glutamate exchanger	328	2E-89
			NP_036376	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 8	326	4E-88
			NP_062823	solute carrier family 7, member 10; asc-type amino acid transporter 1	323	4E-88
			BAA95120	y <sup>+</sup> L amino acid transporter-1	322	1E-87
			AAP05695	L amino acid transporter-2; LAT-2	314	3E-85
			CAD62616	unmatured protein product	210	6E-54
			CAD10393	amino acid transporter	209	1E-53
			NP_620172	amino acid transporter XAT2	207	3E-53
			NP_000565.1	decay accelerating factor for complement (CD55, Clomer blood group system); Decay-	367	1E-101
				accelerating factor of		
			P08174	Complement decay-accelerating factor precursor (CD55 antigen)	365	1E-101
			AAA52167.1	decay-accelerating factor precursor	364	1E-100
			AAB48622.1	decay-acceleration factor	363	1E-100
			A26359	decay-accelerating factor, splice form 1 precursor	355	1E-97
			23200413	Chain R, Structural Model Of Human Decay-Accelerating Factor Bound To Echovirus 7 From	308	8E-64
			AAL25833.1	Cryo-Electron Microscopy	243	6E-64
				decay-accelerating factor 1 ab		
			AAL25835.1	decay-accelerating factor 4ab	243	6E-64
			AAL25834.1	decay-accelerating factor 3	242	7E-64
			NP_001722.1	B-cell translocation protein 1	348	2E-94
			NP_006754.1	BTG family, member 2; B-cell translocation gene 2 (phoechromocytoma cell-3); B-cell	211	3E-53
				translocation gene 2		

5

10

15

20

25

216

NM_022310	Mm.918	F2.11 (7to19)	NP_005138.1	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa); BiP; heat shock 70kD protein 5 (glucose-regulated protein, 78kD); Heat-shock 70kD protein-5 (glucose-regulated protein, 78kD)	1209	0
NP_071705.1			AAF13605.1	BiP protein	1202	0
			A29821	dnaK-type molecular chaperone HSPA5 precursor	1196	0
			XP_088941.1	similar to 78 kDa glucose-regulated protein precursor (GRP 78) (immunoglobulin heavy chain binding protein) (BiP) (Endoplasmic reticulum luminal Ca2+ binding protein grp78)	893	0
			NP_006588.1	heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kD protein 10; heat shock cognate protein 54; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1	770	0
			P08107	Heat shock 70 kDa protein 1 (HSP70.1) (HSP70/HSP70-2)	759	0
			NP_005336.2	heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein; dnaK-type molecular chaperone HSP70-1	759	0
			NP_005337.1	heat shock 70kDa protein 1B; heat shock 70kD protein 1B	758	0
			NP_068814.2	heat shock 70kDa protein 2; heat shock 70kD protein 2; Heat-shock 70kD protein-2	756	0
			AAH36107.1	Unknown (protein for MGC:33922)	754	0
			AAD11466.1	heat shock protein	754	0
			A29160	dnaK-type molecular chaperone HSPA1L	753	0
			XP_175177.1	heat shock 70kD protein 1-like	750	0
			BAA32521.1	Heat shock protein 70 testis variant	750	0
			XP_166348.1	similar to Heat shock 70 kDa protein 1-HOM (HSP70-HOM)	750	0
			NP_005518.1	heat shock 70kDa protein 1-like; Heat-shock 70kD protein-like-1; heat shock 70kD protein 1-like	749	0
			AAH34483.1	heat shock 70kD protein 1-like	747	0

5

10

15

217

			AAH35665.1	heat shock 70kDa protein 6 (HSP70B)	736	0
			NP_002146.1	heat shock 70kDa protein 6 (HSP70B); heat shock 70kD protein 6 (HSP70B); Heat-shock 70kD protein-6 (HSP70B)	735	0
			AAH07276.1	Similar to heat shock cognate 71-kD protein	682	0
			BAB18615.1	heat shock cognate protein 54	600	1E-171
			NP_004125.2	heat shock 70kDa protein 9B (mortalin-2); heat shock 70kD protein 9 (mortalin); mort-2; mhsip75;	574	1E-163
				heat shock 70kD protein 9B (mortalin-2); Heat-shock 70kD protein-9 (mortalin)		
			AAH29926.1	Similar to hypothetical protein FLJ13511	927	0
A K 0 0 4 6 5 4	Mm.86439	F:2.11 (5to19)	AAC18917.1	F02569_2	397	1E-109
BAB23445.1			NP_149014.1	hypothetical protein FLJ13511	335	3E-90
			AAF22843.1	7h3 protein	249	1E-64
			XP_045583.1	similar to Protein KIAA1434	929	0
A K 0 0 9 5 6 3	Mm.28697	F:2.1 (5to19)	BAA92672.1	KIAA1434 protein	929	0
BAB23661.1			BAA91994.1	unnamed protein product	444	1E-124
			NP_062558.1	hypothetical protein R30953_1	233	4E-60
NM_011579	Mm.15793	F:2.1 (5to19)				
NP_035709.1						
NM_021394	Mm.116687	F:2.1 (5to19)	CAC17634.2	dJ71817.3.1 (novel protein similar to mouse tumour stroma and activated macrophage protein	320	4E-87
NP_067369.1				DLM4.1 isoform 1)		

5

10

15

20

218

			NP_110403.1	tumor stroma and activated macrophage protein DLM-1; chromosome 20 open reading frame 183	308	1E-83
			NP_000021.1	alanine-glyoxylate aminotransferase; alanine-glyoxylate aminotransferase, liver-specific	616	1E-176
			NP_057911.1	peroxisomal, serine-pyruvate aminotransferase		
			BAA02632.1	alanine-glyoxylate aminotransferase	614	1E-175
			L70425A	Ala-glyoxylate aminotransferase	609	1E-174
			AAK30157.1	hepatic peroxisomal alanine-glyoxylate aminotransferase	564	1E-160
			NP_003529	H4 histone family, member A	162	8E-41
			NP_038578.1			
			BAB47495	KIAA1866 protein	1197	0
			XP_027638	similar to KIAA1866 protein	1186	0
			NP_005714	tetraspan 5; tetraspan TM4SF; tetraspan NEF-4; transmembrane 4 superfamily member 9; transmembrane 4 superfamily, member 8; tetraspanin 5	566	1E-161
			NP_062517.1			
			AS9261	tetraspan TSPAN-5	552	1E-157
			XP_030395	similar to RIKEN cDNA 2210021[G21] gene [Mus musculus]	447	1E-125
			AAM94899	DC-TMAP2 precursor	338	3E-92
			NP_112189	tetraspanin similar to TM4SF9	337	6E-92
			AAD02920	Similar to transmembrane 4 superfamily member 9	299	2E-80
			AAH44244	Similar to hypothetical protein MGC30714	229	2E-59
			BAB15717	FLJ00016 protein	212	3E-54
			NP_001684.2	ATPase, H+ transporting, lysosomal 56/38kD, V1 subunit B, isoform 2; vacuolar proton pump B isoform 2; endomembrane proton pump 58 kDa subunit; vacuolar ATP synthase subunit B; brain isoform; V-ATPase B2 subunit; H(+)-transporting two-sector ATPase, 56/38kD subunit	1008	0
			NP_007509			
			NP_031535.2			

5

10

15

20

25



219

				isoform 2		
			B44138	H <sup>+</sup> -exporting ATPase (EC 3.6.3.6) 56K chain, vacuolar, brain isoform	1007	0
			AAA58661.1	vacuolar H <sup>+</sup> -ATPase 56,000 subunit	1005	0
			AAH30640.1	ATPase, H <sup>+</sup> transporting, lysosomal 56/58kD, V1 subunit B, isoform 2	1002	0
			AAH07309.1	Unknown (protein for IMAGE:3352651)	990	0
			NP_001683.2	ATPase, H <sup>+</sup> transporting, lysosomal 56/58kD, V1 subunit B, isoform 1; ATPase, H <sup>+</sup> transporting, lysosomal, beta polypeptide, 58kD; vacuolar proton pump, subunit 3; vacuolar ATP synthase subunit B, kidney isoform; V-ATPase B1 subunit; endomembrane proton pump 58 kDa subunit; H(+)-transporting two-sector ATPase, 58kD subunit; H <sup>+</sup> -ATPase beta 1 subunit; ATPase, H <sup>+</sup> transporting, lysosomal 56/58kD, V1 subunit B, isoform 1 (Renal tubular acidosis with deafness)	868	0
			P15133	Vacuolar ATP synthase subunit B, kidney isoform (V-ATPase B1 subunit) (Vacuolar proton pump B isoform 1) (Endomembrane proton pump 58 kDa subunit)	863	0
			AAA36498.1	proton pump 58 kDa subunit	863	0
			A39212	H <sup>+</sup> -transporting ATPase (EC 3.6.1.35), vacuolar	796	0
			AAD11943.1	H <sup>+</sup> -ATPase beta 1 subunit	788	0
			AAH35978.1	Unknown (protein for MGC:32642)	417	1E-115
			NP_000940.1	prolactin receptor	338	1E-124
			NP_032958.1	prolactin receptor short isoform 1a	338	1E-124
			AAD09855.1	intermediate prolactin receptor isoform	338	1E-124

30

35

40

	AAL23914.1		prolactin receptor short isoform 1b	337	1E-125
	AAM11661.1		dela 4-SF1b truncated prolactin receptor	337	1E-92
	AAM18048.1		prolactin receptor delta 7/11	230	7E-92
	pdbj1BP3		Chain A, The Xray Structure Of A Growth Hormone-Prolactin Receptor Complex	242	4E-90
	A57018		prolactin receptor - human	230	1E-86
	AAK32703.1		prolactin receptor isoform delta S1 precursor	271	2E-72
	AAM11660.1		Delta 4-delta 7/11 truncated prolactin receptor	230	8E-61
A K O 3 9 5 0 Mm.36072 BAB23088.1	F:2.09 (Sto19) - AAH36923.1		Similar to RIKEN cDNA 1110029A09 gene	234	1E-60
	BAC04633.1		unnamed protein product	234	1E-60
A K O 1 3 2 5 Mm.5885 NPN_542123.1	F:2.09 (Sto19) NP_004791.1		transmembrane 9 superfamily member 2; 76 kDa membrane protein, transmembrane protein 9 superfamily member 2	1176	0
	NP_055537.1		KIAA0255 gene product	470	1E-125
	AAF98159.1		transmembrane protein TM9SF3	256	2E-68
	XP_030993.1		similar to Transmembrane 9 superfamily protein member 3 precursor (SM-11044 binding protein) (EP70-P-iso)	256	2E-68
	AAF21983.1		SM-11044 binding protein	256	2E-68
	BAB55369.1		unnamed protein product	256	3E-68
	BAA91362.1		unnamed protein product	253	1E-67
	BAC11232.1		unnamed protein product	249	4E-66

221

NP_006396.2				transmembrane 9 superfamily member 1; multispanning membrane protein (70kD); transmembrane protein 9 superfamily member 1	251	4E-63
O15321				Transmembrane 9 superfamily protein member 1 precursor (bMP70)	247	5E-64
NP_002990.1				Syndecan-4 precursor (Amphiglycan) (SYND4) (Ryndocan core protein)	238	2E-62
NP_002990.1				syndecan 4 (amphiglycan, ryndocan)	238	2E-62
NP_060809.2				hypothetical protein FLJ111149	308	3E-83
BAA92033.1				unnamed protein product	306	1E-82
NP_000774.2				cytochrome P450, subfamily XXVIA, polypeptide 1, isoform 1; P450, retinoic acid-inactivating, 1; retinoic acid-metabolizing cytochrome; retinoic acid 4-hydroxylase	901	0
O43174				Cytochrome P450 26 (Retinoic acid-metabolizing cytochrome) (P450RA1) (Retinoic acid 4-hydroxylase)	896	0
NP_476498.1				cytochrome P450, subfamily XXVIA, polypeptide 1, isoform 2; P450, retinoic acid-inactivating, 1; retinoic acid-metabolizing cytochrome; retinoic acid 4-hydroxylase	813	0
NP_063938.1				cytochrome P450 retinoid metabolizing protein	391	1E-107
S29028				aspartate transaminase (EC 2.6.1.1) (clone 8C7)	810	0
S13035				aspartate transaminase (EC 2.6.1.1)	779	0
NP_002070.1				aspartate aminotransferase 1, glutamic-oxaloacetic transaminase 1, soluble	779	0
AAH00525.1				glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)	395	1E-109
NP_002173.1				interleukin 1 receptor accessory protein isoform 1	1028	0

၆

70

15

20

222

NP_03290.1					NP_608273.1	interleukin 1 receptor accessory protein isoform 2	645	0
					NP_059112.1	interleukin 1 receptor accessory protein-like 2; interleukin 1 receptor 9; IL-1 receptor; X-linked interleukin-1 receptor accessory protein-like 2; IL-1 receptor accessory protein-like 2	320	1E-85
					AAF59412.1	X-linked interleukin-1 receptor accessory protein-like 2	319	2E-85
NM_023380	Mm.133330	F2.08 (5019)	P21709			Ephrin type-A receptor 1 precursor (Tyrosine-protein kinase receptor Eph)	1040	0
NP_076069.1			A34076			protein-tyrosine kinase (EC 2.7.1.112) receptor type eph 1 precursor	1573	0
			NP_005223.1			EphA1; eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence; oncogene Eph; ephrin receptor EphA1); eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence); ephrin receptor EphA1	1569	0
			S44280.			receptor tyrosine kinase epb	1179	0
			AAH37166.1			EphA2	874	0
			NP_004422.1			EphA2; ephrin receptor EphA2; epitelial cell receptor protein tyrosine kinase	867	0
			NP_004431.1			EphA7; Hek11; ephrin receptor EphA7	790	0
			NP_004429.1			EphA4; Hek8; TYRO1 protein tyrosine kinase; ephrin receptor EphA4	778	0
			178843			receptor protein-tyrosine kinase - human (fragment)	773	0
			XP_040083.2			similar to Ephrin type-A receptor 5 precursor (Tyrosine-protein kinase receptor EHK-1) (Eph homology kinase-1) (Receptor protein-tyrosine kinase HEK7)	770	0
			P54756			Ephrin type-A receptor 5 precursor (Tyrosine-protein kinase receptor EHK-1) (Eph homology kinase-1) (Receptor protein-tyrosine kinase HEK7)	768	0
			P29320			Ephrin type-A receptor 3 precursor (Tyrosine-protein kinase receptor ETK-1) (HEK) (HEK-4)	762	0
			NP_005224.2			EphA3; Ephrin receptor EphA3 (human embryo kinase 1); eph-like tyrosine kinase 1 (human embryo kinase 1); ephrin receptor EphA3	759	0
			NP_004432.1			ephrin receptor EphB1 precursor; eph tyrosine kinase 2; ephrin receptor EphB1	708	0

5

10

15

20

223

NP_004434.2	ephrin receptor EphB3 precursor; human embryo kinase 2; EPH-like tyrosine kinase 2; tyrosine-protein kinase receptor HEK-2	702	0
AAD02030.1	Eph-like receptor tyrosine kinase hEphB1	701	0
NP_065387.1	ephrin receptor EphA8 precursor; ephrin type-A receptor 8 precursor; eph- and elk-related tyrosine kinase; tyrosylprotein kinase; tyrosine-protein kinase receptor eefc protein-tyrosine kinase; hydroxyaryl-protein kinase	699	0
P54753	Ephrin type-B receptor 3 precursor (Tyrosine-protein kinase receptor HEK-2)	696	0
AAD02031.1	Eph-like receptor tyrosine kinase hEphB1b	691	0
I78842	receptor protein-tyrosine kinase - human (fragment)	687	0
P29323	Ephrin type-B receptor 2 precursor (Tyrosine-protein kinase receptor EPH-3) (DRT) (Receptor protein-tyrosine kinase HEK3) (ERK)	686	0
AAA99310.1	protein-tyrosine kinase	686	0
NP_059145.1	ephrin receptor EphB2 isoform 1 precursor; developmentally-regulated eph-related tyrosine kinase; elk-related tyrosine kinase; eph tyrosine kinase 3	686	0
BAA06506.1	tyrosine kinase precursor	685	0
NP_004435.2	ephrin receptor EphB4 precursor; Ephrin receptor EphB4 (hepatoma transmembrane kinase); Tyro11; ephrin receptor EphB4; hepatoma transmembrane kinase	656	0
AA020598.1	tyrosine kinase	656	0
P54760	Ephrin type-B receptor 4 precursor (Tyrosine-protein kinase receptor HTK)	656	0
AAB94627.1	Eph-like receptor tyrosine kinase hEphB1c	650	0
AA114195.1	receptor protein tyrosine kinase variant EphB4v1	606	1E-173
NP_004436.1	ephrin receptor EphB6 precursor; tyrosine-protein kinase-defective receptor; ephrin type-B receptor 6	598	1E-170

5

10

15

224

			AAH04264.1	Similar to EphB4	594	1E-169
			BAA95983.1	KIAA1459 protein	592	1E-168
			AAD03058.1	Eph-family protein	447	1E-125
			CAC10350.1	dJ74M1.1.1 (tyrosine kinase isoform 1)	399	1E-110
			CAC10351.1	dJ74M1.1.2 (tyrosine kinase isoform 2)	399	1E-110
			A37174	protein-tyrosine kinase (EC 2.7.1.112) erk - human (fragment)	394	1E-109
			AAG43577.1	ephrin receptor EPHA3 secreted form	385	1E-106
			BAA03377.1	large erk kinase	351	4E-96
			CAK66265	phosphatase 2a	635	0
			NP_004563	phosphatase 2	614	1E-174
			NP_103589.2	phosphatase related; resiniferatoxin-binding, phosphatase-related gene, phosphatase-related	630	1E-180
			AAK14923.1	HPTRP	627	1E-179
			AAH00341.1	signal sequence receptor, beta (translocin-associated protein beta)	339	5E-93
			NP_003136.1	signal sequence receptor, beta precursor; Signal sequence receptor, beta; translocin-associated protein beta	337	2E-92
			NP_000304.1	protein S (alpha) Protein S, alpha	1092	0

5

10

15

20

225

			P07225	Vitamin K-dependent protein S precursor	1092	0
			AAA60180.1	protein S alpha	1092	0
			CAA31383.1	pre-protein S (AA -15 to 635)-tg start	1082	0
			AAA60181.1	protein S precursor	1082	0
			NP_000811.1	growth arrest-specific 6; AXL stimulatory factor	548	1E-154
M12573	Mm.6388	P:2.07 (5to19)	NP_005536.2	heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein; dnaK-	347	2E-94
AAA37863.1				Type molecular chaperone HSP70-1		
			P08107	Heat shock 70 kDa protein 1 (HSP70.1) (HSP70.1/HSP70.2)	347	2E-94
			NP_005537.1	heat shock 70kDa protein 1B; heat shock 70kD protein 1B	345	6E-94
			A29160	dnaK-type molecular chaperone HSPAIL	341	2E-92
			XP_175177.1	heat shock 70kD protein 1-like	312	6E-84
			NP_005518.1	heat shock 70kDa protein 1-like; Heat-shock 70kD protein-like-1; heat shock 70kD protein-like 1; heat shock 70kD protein 1-like	311	1E-83
			BAA32521.1	Heat shock protein 70 testis variant	310	3E-83
			XP_166348.1	similar to Heat shock 70 kDa protein 1-HOM (HSP70-HOM)	310	3E-83
			AAH44483.1	heat shock 70kD protein 1-like	308	1E-82
			AAH07276.1	Similar to heat shock cognate 71-kd protein	301	1E-80
			AAH15699.1	Unknown (protein for IMAGE:3906958)	301	1E-80
			NP_006588.1	heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kD protein 10; heat shock cognate protein 54; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1	301	1E-80

5

10

15

226

			AAH08907.1	Similar to heat shock 70kD protein 8	301	1E-80
			NP_068814.2	heat shock 70kDa protein 2; heat shock 70kD protein-2	300	3E-80
			AAH36107.1	Unknown (protein for MGC:33922)	300	3E-80
			AAD11466.1	heat shock protein	300	3E-80
			CAA36062.1	heat shock protein 70B' (AA 355-643)	285	1E-75
			XP_084070.5	similar to HEAT SHOCK 70 KD PROTEIN 6 (HEAT SHOCK 70 KD PROTEIN B)	285	1E-75
			AAH35665.1	heat shock 70kDa protein 6 (HSP70B')	285	1E-75
			NP_002146.1	heat shock 70kDa protein 6 (HSP70B'); heat shock 70kD protein 6 (HSP70B'); Heat-shock 70kD protein-6 (HSP70B')	285	1E-75
			P01028	Complement C4 precursor [Contains: C4A anaphylatoxin]	2587	0
			C4HU	complement C4A precursor [validated]	2586	0
			NP_009224.1	complement component 4A preproprotein; acidic C4; Rodgers form of C4; complement component 4S	2583	0
			CAB89302.1	dJ34F7.4 (complement component 4A)	2582	0
			NP_000583.1	complement component 4B preproprotein; Chido form of C4; basic C4; complement component 4F	2581	0
			AAB59337.1	complement component C4A	2563	0
			AAA99717.1	complement C4B precursor	2465	0
			NP_000055.1	complement component 3 precursor	624	1E-178
			AAA59611.1	complement component C4B	573	1E-163

5

10

15



227

				NP_001726.1	complement component 5	479	1E-134
				1000226A	complement C4d	436	1E-121
				1006226B	complement C4d variant	430	1E-119
				AAC98380.1	complement protein C4B frameshift mutant	421	1E-117
				AAA51856.1	complement component C5	346	1E-100
U 2 7 3 1 5							
AA052837.1				XP_003631.3	similar to ADP,ATP carrier protein, heart/skeletal muscle isoform T1 (ADP/ATP translocase 1)	553	1E-157
				NP_001143.1	(Adenine nucleotide translocator 1) (ANT1)		
				NP_001142.1	solite carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 4;	540	1E-153
				NP_001143.1	adenine nucleotide translocator 1 (skeletal muscle)		
				NP_001143.1	solite carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5; 2F1;	525	1E-149
				XP_114724.1	adenine nucleotide translocator 2 (fibroblast)		
				XP_114724.1	similar to ADP,ATP carrier protein, liver isoform T2 (ADP/ATP translocase 3) (Adenine nucleotide translocator 3) (ANT 3)	523	1E-148
				A29132	ADP,ATP carrier protein T2	523	1E-148
				AA096347.1	ADP/ATP carrier protein (adenine nucleotide translocator 2)	522	1E-148
				AAH14775.1	Similar to solite carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5	521	1E-148
				B28116	ADP,ATP carrier protein (clone pHAT8) - human	462	1E-130
				AAA36749.1	ADP,ATP translocase	448	1E-126
				NP_112581.1	hypothetical protein DKFZp434N1235	415	1E-116
				XP_065814.1	similar to ADP,ATP carrier protein, fibroblast isoform (ADP/ATP-translocase 2) (Adenine nucleotide translocator 2) (ANT 2)	335	6E-92
				XP_070893.1	similar to ADP,ATP carrier protein, liver isoform T2 (ADP/ATP translocase 3) (Adenine nucleotide translocator 3) (ANT 3)	328	1E-89
				XP_170195.1	similar to ADP,ATP carrier protein, fibroblast isoform (ADP/ATP-translocase 2) (Adenine nucleotide translocator 2) (ANT 2)	309	5E-84

5

10

15

20

228

					nucleotide translocator 2) (ANT 2)		290	2E-78
					XP_095833.1 similar to ADP/ATP carrier protein			
					XP_167013.1 similar to ADP <sub>i</sub> -ATP carrier protein, fibroblast isoform (ADP/ATP translocase 2) (Adenine nucleotide translocator 2) (ANT 2)		255	1E-67
					XP_167333.1 similar to ADP <sub>i</sub> -ATP carrier protein, fibroblast isoform (ADP/ATP translocase 2) (Adenine nucleotide translocator 2) (ANT 2)		218	2E-56
					XP_063000.2 similar to ADP/ATP carrier protein		196	6E-50
							417	1E-115
NM_007866.0	Mm.2774	F:2.06 (7to19)	P49895		Type I iodothyronine deiodinase (Type-I 5-deiodinase) (DIO1) (Type 1 D1) (SD1)			
NP_031886.1			NP_000783.2		thyroxine deiodinase type I; 5DI; thyroxine deiodinase type I (selenoprotein)		409	1E-113
							207	4E-52
					AAH17955.1 Similar to deiodinase, iodothyronine, type I			
							224	2E-58
NM_020000.1	Mm.117121	F:2.06 (5to19)	NP_569708.1		dendritic cell lectin b; blood dendritic cell antigen 2 protein			
NP_064385.1								
							300	6E-82
NM_026533	Mm.14798	F:2.05 (5to19)	NP_001008.1		ribosomal protein S13; 40S ribosomal protein S13			
NP_080809.1							225	3E-59
					AAC15854.1 ribosomal protein S13			
							598	1E-171
NM_033373	Mm.20127	F:2.05 (YtoO)	BAA92054		unnamed protein product			
NP_203537.1							597	1E-170
							593	1E-169
							591	1E-169

25

30

35

40

229

TI17294	hypothetical protein DKFZp34G032.1	322	7E-88
NP_775320	keratin 23 isoform b; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cyokeratin 23; type I intermediate filament cyokeratin; histone deacetylase inducible keratin 23	321	2E-87
S37780	keratin 20, type I-like, cytoskeletal	299	6E-81
XP_049979	similar to Keratin, type I cytoskeletal 20 (Cyokeratin 20) (K20) (CK 20)	299	8E-81
P08727	Keratin, type I cytoskeletal 19 (Cyokeratin 19) (K19) (CK 19)	287	3E-77
NP_002267	keratin 19; keratin, type I cytoskeletal 19; keratin, type I, 40-kD; cyokeratin 19; 40-kDa keratin	287	3E-77
	intermediate filament precursor gene		
BAC04534	unnamed protein product	287	3E-77
NP_000413	keratin 17	287	3E-77
KRH09	keratin 19, type I, cytoskeletal	286	7E-77
NP_000214	keratin 12 (Meesmann corneal dystrophy); Keratin-12; keratin 12	283	4E-76
NP_002266	keratin 15; keratin-15, basic; keratin-15, beta; type I cytoskeletal 15; cyokeratin 15	283	4E-76
P19012	Keratin, type I cytoskeletal 15 (Cyokeratin 15) (K15) (CK 15)	283	4E-76
NP_002265	keratin 13 isoform b; keratin, type I cytoskeletal 13; cyokeratin 13	281	2E-75
NP_705694	keratin 13 isoform a; keratin, type I cytoskeletal 13; cyokeratin 13	281	2E-75
KRH03	keratin 13, type I, cytoskeletal, long splice form	281	2E-75
AAA59460	keratin type 16	278	1E-74
NP_005548	keratin 16; keratin, type I cytoskeletal 16; cyokeratin 16	278	2E-74
JC4313	keratin 16, type I, cytoskeletal	278	2E-74
KRHUE	keratin 14, type I, cytoskeletal	277	3E-74
AAH02690	keratin 14 (epidermolysis bullosa simplex, Dowling-Mearns, Koeber)	277	3E-74
NP_005317	keratin 14; cyokeratin 14	277	3E-74
NP_003762	type I hair keratin 6; keratin, hair, acidic, 6	264	3E-70
AAH43581	Similar to keratin, hair, acidic, 6	264	3E-70
	cyokeratin 20	263	4E-70
CAA51914	type I hair keratin 5; Ha-5; hard keratin, type I, 5	257	3E-68
NP_002271	hypothetical protein FLJ20261	256	6E-68
NP_061889	type I hair keratin 5	256	8E-68
CAA76387	keratin, type I cuticular HA5 (Hair keratin, type I HA5)	256	8E-68
Q22764	IFHa5 hair keratin type I intermediate filament	256	8E-68
CAA62286	similar to keratin 17	253	5E-67
XP_039921	keratin 10 (epidermolysis hyperkeratosis; keratosis palmaris et plantaris)	252	9E-67

5

10

15

20

25

30

230

		PI3645	Keratin, type I cytoskeletal 10 (CytoKeratin 10) (K10) (CK 10).	252	9E-67
		XP_170564	similar to keratin 17	252	9E-67
		NP_004129	type I hair keratin 3A; Ha-3H; hard keratin, type 1,3; keratin, hair, acidic, 3A	251	2E-66
		O76009	Keratin, type I cuticular HA3-1 (Hair keratin, type I HA3-1).	251	3E-66
		KRHL0	keratin 10, type I, cytoskeletal	250	3E-66
5		NP_002268	type I hair keratin 1; hard keratin, type I, 1, Ha-1; keratin, hair, acidic, 1	249	6E-66
		Q15323	Keratin, type I cuticular HA1 (Hair keratin, type I HA1).	249	7E-66
		O76011	Keratin, type I cuticular HA4 (Hair keratin, type I HA4).	248	1E-65
		NP_002270	type I hair keratin 3B; keratin, hair, acidic, 3B; Ha-3H; hard keratin, type 1, 3H	248	2E-65
10		S60034	keratin HA1, type I, hair	247	4E-65
		CAA57956	hair keratin acidic 3-II	246	5E-65
		AAH41070	similar to keratin, hair, acidic, 4	246	6E-65
		NP_066293	type I hair keratin 4; hard keratin, type I, 4	245	1E-64
		NP_002269	type I hair keratin 2; Ha-2; hard keratin, type I, 2; keratin, hair, acidic, 2	245	1E-64
15		XP_091665	similar to RIKEN cDNA 4733401L19 [Mus musculus]	244	2E-64
		Q14532	Keratin, type I cuticular HA2 (Hair keratin, type I HA2).	244	2E-64
		CAA57179	hair type I acidic keratin	244	2E-64
		NP_000215	keratin 18	243	4E-64
		CAA82315	cytoKeratin 9	243	7E-64
20		CAA31377	cytoKeratin 18 (424 AA)	243	7E-64
		NP_000217	keratin 9; Keratin-9	243	7E-64
		J37459	keratin Ha3-II, type I, hair - human	242	9E-64
		AAH00698	Keratin 18	242	1E-63
		AAA59468	keratin-10	239	6E-63
25		CAA76389	type I hair keratin 7	236	5E-62
		NP_000412	keratin 10; Keratin-10	236	5E-62
		O76015	Keratin, type I cuticular HA8 (Hair keratin, type I HA8).	236	6E-62
		NP_006762	type I hair keratin 8	236	6E-62
		AAH09754	Similar to keratin 18	233	4E-61
30		NP_003761	type I hair keratin 7	232	9E-61
		BAC03847	unnamed protein product	216	9E-56
		NP_004660	chloride intracellular channel 3	380	1E-105
		AK009020	Mm44194		
		BAB260302			

231

			O15247	Chloride intracellular channel protein 2 (XAP121)	229	3E-60
			AA122305	chloride intracellular channel 2	229	3E-60
			CAA73228	p64 bovine chloride channel-like protein	228	9E-60
			NP_001280	chloride intracellular channel 2	228	9E-60
			CAA03948	CLIC2	227	1E-59
			NP_001279	chloride intracellular channel 1; p64CLCP	226	2E-59
			AA025675	nuclear chloride ion channel protein	225	3E-59
			Q9NZA1	Chloride intracellular channel protein 5	224	8E-59
			BAC11444	unnamed protein product	224	8E-59
			NP_058625	chloride intracellular channel 5	224	8E-59
			NP_039234	chloride intracellular channel 4; chloride intracellular channel 4 like	224	1E-58
			NP_444507	chloride intracellular channel 6; chloride channel form A	223	2E-58
			IK00A	Chain A, Crystal Structure Of A Soluble Form Of ClC1, An Intracellular Chloride Ion Channel	223	3E-58
			AAK52083	CLIC5B	222	5E-58
			AAD38446	H1 chloride channel; p64H1; CLIC4	221	7E-58
			AAD26136	intracellular chloride channel p64H1	219	3E-57
			AAAT6730	chloride channel form B	217	2E-56
			CAC36880	hA802N13.1.1 (chloride intracellular channel 5; isoform 1)	215	5E-56
			BAA91794	unnamed protein product	195	7E-50
NM_025939	Mm.182931	F:2.05 (7n11)	NP_006443.1	phosphoribosylaminimidazole carboxylase; phosphoribosylaminimidazole succinocarboxamide synthetase; phosphoribosylaminimidazole carboxylase,	839	0
NP_080215.1				phosphoribosylaminimidazole succinocarboxamide synthetase		
			XP_094990.1	similar to Multifunctional protein ADE2	310	4E-84
			XP_116650.2	similar to Multifunctional protein ADE2	305	2E-82
J 0 4 6 9 4	Mm.738	F:2.05 (5n11)	1402236A	collagen alpha (IV)	563	1E-159
AAA50292.1			NP_001836.1	alpha 1 type IV collagen preproprotein; collagen IV, alpha-1 polypeptide; collagen of basement membrane, alpha-1 chain	563	1E-159

5

10

15

20

25

232

			GAC13153.1	bA472K17.2 (collagen type IV alpha 1)	563	1E-159
			CAA68698.1	alpha1-chain	520	1E-146
			AAA52042.1	procollagen alpha-1 type IV	479	1E-133
			AAA52006.1	pro-alpha-1(IV)	479	1E-133
			pdh1111	Chain A, The 1.9-A Crystal Structure Of The Noncollagenous (NC1) Domain Of Human Placenta Collagen IV Shows Stabilization Via A Novel Type Of Covalent Met-Lys Cross-Link	474	1E-132
			AAM97359.1	arresten	470	1E-130
			CAB00289.1	dA24A23.1 (collagen, type IV, alpha 5 (Alport syndrome))	422	1E-116
			AAA52045.1	collagen type IV alpha 5 chain	422	1E-116
			AAA99480.1	alpha-5 type IV collagen	422	1E-116
			NP_203699.1	alpha 5 type IV collagen, isoform 2, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	422	1E-116
			NP_203700.1	alpha 5 type IV collagen, isoform 3, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	422	1E-116
			NP_000486.1	alpha 5 type IV collagen, isoform 1, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain	422	1E-116
			AAA51558.1	alpha-5 type IV collagen	422	1E-116
			AAA51556.1	alpha-3 type IV collagen	362	3E-98
			AAA21610.1	alpha-3 type IV collagen	362	3E-98
			AAF72632.1	tunstatin	362	3E-98
			NP_000082.1	alpha 3 type IV collagen, isoform 1, precursor; collagen IV, alpha-3 polypeptide (goodpasture antigen)	362	3E-98

5

10

15

233

		CGHUB3	collagen alpha 3(IV) chain precursor, long splice form	362	3E-98
		CAC36101.1	a3 type IV collagen	362	3E-98
		CAA29075.1	alpha-1 chain precursor (AA-27 to 917) (2953 is 2nd base in codon)	357	2E-96
		AAB19637.1	type IV collagen alpha 3 chain	349	3E-94
		pdj111	Chain A, The 1.9-A Crystal Structure Of The Noncollagenous (NC1) Domain Of Human Placenta	322	4E-86
		P08572	Collagen Iv Shows Stabilization Via A Novel Type Of Covalent Met-Lys Cross-Link	322	4E-86
		NP_001837.1	Collagen alpha 2(IV) chain precursor	322	4E-86
			alpha 2 type IV collagen preproprotein; canstatin	322	4E-86
		CAA29098.1	alpha (2) chain	322	4E-86
		AAAS2043.1	alpha-2 type IV collagen	321	8E-86
		AAAS8422.1	collagen alpha-2 type IV	320	1E-85
		AAF72631.1	canstatin	320	1E-85
		CAA20120.1	COL4A6 (Collagen Alpha 6(IV))	307	1E-81
		AAB19038.1	collagen type IV a6 chain	307	1E-81
		NP_001838.1	type IV alpha 6 collagen, isoform A precursor; collagen IV, alpha-6 polypeptide; collagen of	307	1E-81
		Q14031	basement membrane, alpha-6	307	1E-81
		NP_378667.1	Collagen alpha 6(IV) chain precursor	307	1E-81
			type IV alpha 6 collagen, isoform B precursor; collagen IV, alpha-6 polypeptide; collagen of	307	1E-81
		AAB19039.1	basement membrane, alpha-6	307	1E-81
			collagen type IV a6 chain	307	1E-81

234

U70139	Mm.86541	F:2.05 (5to7)	NP_036250.1	CCR4 carbon catabolite repression 4-like ( <i>S. cerevisiae</i> ); CCR4-like (carbon catabolite repression 4, <i>S. cerevisiae</i> )	603	1E-170
AAB62717.1			AAG01389.1	nocturnin	554	1E-155
			AAM81188.1	pol protein	375	1E-150
			AAK11553.1	polymerase	330	1E-132
			AAD51797.1	Gag-Pro-Pol protein	330	1E-132
			AAD21097.1	polymerase	330	1E-132
			AA88031.1	pol/env ORF (bases 3878-8257) first start codon at 4172; Xxx; putative	327	1E-131
			AAK11554.1	polymerase	327	1E-131
			P10266	Endogenous retrovirus HERV-K10 putative pol polyprotein [Includes: Reverse transcriptase; Endonuclease]	327	1E-131
			AAD51793.1	Gag-Pro-Pol-Env protein	327	1E-130
			AAD51796.1	Gag-Pro-Pol protein	312	1E-126
			AA160056.	pol protein	312	1E-126
			AA001388.	nocturnin	414	1E-113
			AAG18012.	gag-pro-pol precursor	252	1E-113
			AAC63294.1	polymerase	167	3E-70
			AAC63291.1	polymerase	166	8E-69
			AAC63292.1	polymerase	166	1E-68
			AAC63293.1	polymerase	163	2E-68
			AAC63290.1	polymerase	164	3E-68

5

10

15

20



235

NM_008956	Mm.19117	F:2.05 (5to19)	NP_114368.1	polypyrimidine tract binding protein, isoform c; RNA binding protein; heterogeneous nuclear ribonucleoprotein I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)	840	0
NP_032982.1						
			NP_114367.1	polypyrimidine tract binding protein, isoform b; RNA binding protein; heterogeneous nuclear ribonucleoprotein polypeptide I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)	828	0
			NP_002810.1	polypyrimidine tract binding protein, isoform a; RNA binding protein; heterogeneous nuclear ribonucleoprotein polypeptide I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)	826	0
			BAB71742.1	PTB-like protein L	674	0
			AA094624.1	non-neuronal splice variant nPTB3	670	0
			NP_067013.1	polypyrimidine tract binding protein 2; neural polypyrimidine tract binding protein; PTB-like protein	668	0
			AA094625.1	non-neuronal splice variant nPTB4	664	0
			NP_051471.1	ROD1 regulator of differentiation 1; fission yeast differentiation regulator; regulator of differentiation (in S. pombe) 1	640	0
			BAB71743.1	PTB-like protein S	426	1E-118
			XP_063346.3	similar to polypyrimidine-tract binding protein	410	1E-114
			pdj1Q09	Chain A, Non-Representative Structure	312	2E-84
NM_011919	Mm.25709	F:2.05 (5to19)	AA07921.1	p3JING1b	435	1E-122
NP_036049.1						

236

			AAG02578.1	growth inhibitory protein ING1	434	1E-122
			AAC00501.1	candidate tumor suppressor p33ING1	431	1E-121
			AAG02579.1	growth inhibitory protein ING1	347	9E-96
			NP_005528.2	inhibitor of growth family, member 1; inhibitor of growth 1 family, member 1	347	9E-96
			AAF37423.1	ING1 tumor suppressor, variant C	343	2E-94
			AAB60879.1	p33ING1	343	2E-94
			BAA82887.1	p47	343	2E-94
			BAA82889.1	p33	341	7E-94
			BAB08103.1	p24ING1c	309	4E-84
			BAA83462.1	p24 is an alternatively spliced transcript of p33/ING1.	305	7E-83
			CAC20567.1	p32 protein	281	8E-76
			NP_001555.1	inhibitor of growth 1-like	281	1E-75
NM_019447	Mm.27369	F:2.05 (5to19)	NP_001519.1	HGF activator	1048	0
NP_062320.1			CAA93803.1	hepatocyte growth factor (HGF) precursor	1041	0
			NP_000496.1	coagulation factor XII precursor, Hageman factor	462	1E-129
			AAA51986.1	coagulation factor XII	462	1E-129
			AAA70225.1	coagulation factor XII precursor	462	1E-129

237

			AAA70224.1	human factor XII	370	1E-102
			BAA00831.1	tissue plasminogen activator	305	1E-82
			NP_000921.1	plasminogen activator, tissue type isoform 1 preproprotein; plasminogen activator, tissue type; t-plasminogen activator; alteplase; reteplase	305	1E-82
			AAB59510.1	plasminogen activator	303	6E-82
			NP_004123.1	hyaluronan binding protein 2; hyaluronic acid binding protein 2; hepatocyte growth factor activator-like protein; plasma hyaluronan binding protein	300	7E-81
			NP_127509.1	plasminogen activator, tissue type isoform 3 precursor; plasminogen activator, tissue type; t-plasminogen activator; alteplase; reteplase	298	2E-80
S 6 7 3 8 6	NULL	F2.05 (5to19)	NP_004648.1	serum deprivation response protein; serum deprivation response; phosphatidylserine-binding protein	611	1E-174
AAB28933.1						
			AAG77093.1	leucine-zipper protein FKSG13	215	3E-55
NM_008039	Mm.57142	F2.04 (YtoO)	NP_001453	formyl peptide receptor-like 1; lipoxin A4 receptor (formyl peptide receptor related)	502	1E-142
NP_032065.1						
			AAAS8481	fMLP-related receptor II	501	1E-142
			AAAS2474	DEFINITION N-formyl peptide receptor-like 2 protein	419	1E-117
			NP_002021	formyl peptide receptor-like 2	415	1E-116
			NP_002020	formyl peptide receptor 1	410	1E-114
			P21462	fMet-Leu-Phe receptor (fMLP receptor) (N-formyl peptide receptor) (FPR) (N-formylpeptide chemottractant receptor)	407	1E-113
			A42009	N-formyl peptide receptor	6	1E-113
			AAAS36362	N-formylpeptide receptor fMLP-R98	404	1E-113
			AACS1258	orphan G-protein coupled receptor Dez isoform a	201	1E-51
			NP_004063	chemokine-like receptor 1	201	2E-51

5

10

15

20

238

[illegible]

5

10

15

20

25

30

## 239

			NP_653252	hypothetical protein FI125471	296 1E-79
NM_007472	Mm.18625	F:2.04 (7to11)	152366	urine water channel	496 1E-140
NP_031498.1			AAH22486.1	aquaporin 1 (channel-forming integral protein, 28kD)	495 1E-139
			NP_000376.1	aquaporin 1; aquaporin 1 (channel-forming integral protein, 28kDa); Aquaporin-1 (channel-forming integral protein, 28kDa); Colton blood group	495 1E-139
			AAI87136.1	aquaporin 1	488 1E-137
			AAC50649.1	channel-like integral membrane protein	293 7E-79
			AAC23788.1	aquaporin	276 8E-74
			AAC03168.1	putative alternative lens membrane intrinsic protein	238 2E-62
			NP_036196.1	major intrinsic protein of lens fiber; aquaporin	233 1E-60
			NP_000477.1	aquaporin 2; Aquaporin-2 (collecting duct)	230 9E-60
			AAB30268.1	EAQP-CD=collecting duct aquaporin [human, kidney, Peptide, 271 aa]	228 3E-59
			I51877	water-channel aquaporin 2	227 7E-59
			I64818	water-channel aquaporin 2	227 7E-59
			AAC16481.1	aquaporin (water channel protein)	223 1E-57
			NP_004019.1	aquaporin 4 C2 isoform; mercurial-insensitive water channel	221 3E-57
			NP_001641.1	aquaporin 4 isoform a; mercurial-insensitive water channel	221 3E-57
			I39177	mercurial-insensitive water channel	221 4E-57
			I39178	aquaporin 4, long splice form	221 4E-57
			NP_001642.1	aquaporin 5; Aquaporin-5	218 5E-56

240

NM_029239	Mm.108609	F:2.04 (7to11)	NP_005804.1	protein kinase C, $\alpha$ , serine-threonine protein kinase	594	1E-170
NP_083515.1			AAH30706.1	Similar to protein kinase C, $\alpha$	592	1E-169
			NP_002733.1	protein kinase C, $\alpha$	378	1E-105
			NP_057541.2	protein kinase D2	342	6E-94
			BAC11508.1	unnamed protein product	218	2E-56
			BAC11127.1	unnamed protein product	218	2E-56
AK003830	Mm.279	F:2.04 (7to19)	NP_057146.1	CGI-128 protein *	208	4E-80
BAB2024.1						
NM_020520	Mm.29666	F:2.04 (7to19)	CAB55356.1	carnitine/acylcarnitine translocase	582	1E-166
NP_065266.1			NP_000378.1	carnitine/acylcarnitine translocase; Carnitine-acylcarnitine translocase; carnitine-acylcarnitine carrier, solute carrier family 25 (carnitine/acylcarnitine translocase), member 20	581	1E-166
AK007264	Mm.200370	F:2.04 (5to19)	AAD12227.1	similar to uridine phosphorylase; similar to Q16831 (P1D:g2494059)	447	1E-125
BAB24924.1			XP_087230.2	similar to Uridine phosphorylase (UDRPase)	428	1E-120
			NP_003355.1	uridine phosphorylase	316	3E-86
AK008088	Mm.10706	F:2.04 (5to19)	NP_116024.1	seven transmembrane domain protein	442	1E-123
BAB25453.1						
			CAA77013.1	seven transmembrane domain protein	414	1E-115

5

10

15

20

241

NM_011017	Mm.200907	F:2.04 (5to19)	AAG17977.1	unknown		561	1E-159
NP_035147.1			NP_055067.1	ornithine transporter 1 (hyperornithinemia-hyperammonemia-homocitrullinuria); ornithine transporter 1		560	1E-159
			NP_114153.1	ornithine transporter 2		499	1E-141
			AAM94902.1	ornithine transporter 2		497	1E-140
NM_029796	Mm.176946	F:2.04 (5to19)	NP_443204.1	leucine-rich alpha-2-glycoprotein		330	3E-90
NP_084072.1			NBHUA2	leucine-rich alpha-2-glycoprotein		329	6E-90
			AAH34389.1	leucine-rich alpha-2-glycoprotein		327	2E-89
NM_021532	Mm.46662	F:2.03 (YtoO)	NP_057735	DAPPER1; hepatocellular carcinoma novel gene 3		970	0
NP_067507.2			AAF65569	hepatocellular carcinoma novel gene-3 protein		714	0
			CAD61905	unannotated protein product		714	0
NM_011087	Mm.193462	F:2.03 (YtoO)	NP_077294	immunoglobulin-like transcript 8		407	1E-113
NP_035217.1			AAC51892	immunoglobulin-like transcript 5 protein		400	1E-111
			AAC51902	immunoglobulin-like transcript 5		400	1E-111
			AAC51893	immunoglobulin-like transcript 5 protein		400	1E-111
			AAB88120	immunoglobulin-like transcript 5; IL75		399	1E-110
			AAB87667	leucocyte immunoglobulin-like receptor-3; LIR-3		399	1E-110
			AAC51888	immunoglobulin-like transcript 5 protein		399	1E-110
			AAC51894	immunoglobulin-like transcript 5 protein		399	1E-110
			AAC51889	immunoglobulin-like transcript 5 protein		399	1E-110

5

10

15

20

25

242

	AAC51895	immunoglobulin-like transcript 5 protein	399	1E-110
	AAC51901	immunoglobulin-like transcript 5	397	1E-110
	NP_006855	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 3;	396	1E-109
		leukocyte immunoglobulin-like receptor 3		
	AAC51896	immunoglobulin-like transcript 5 protein	396	1E-109
	AAC51890	immunoglobulin-like transcript 5 protein	395	1E-109
	AAC51891	immunoglobulin-like transcript 5 protein	395	1E-109
	AAC51900	immunoglobulin-like transcript 5	394	1E-109
	AAC51897	immunoglobulin-like transcript 5 protein	394	1E-109
	AAC51887	immunoglobulin-like transcript 5 protein	393	1E-109
	NP_036408	immunoglobulin-like transcript 7	393	1E-108
	AAL36993	immunoglobulin-like transcript-7	382	1E-105
	AAC51178	immunoglobulin-like transcript 1c	382	1E-105
	AAD50364	immunoglobulin-like transcript 1c	382	1E-105
	AAD17990	immunoglobulin-like transcript 1c variant 3	380	1E-105
	AAD50365	immunoglobulin-like transcript 1c	380	1E-105
	AAD17991	immunoglobulin-like transcript 1c variant 4	380	1E-105
	AAC51176	immunoglobulin-like transcript 1a	376	1E-103
	JCS897	killer cell inhibitory receptor p91 precursor	376	1E-103
	NP_006854	leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 1; leukocyte immunoglobulin-like receptor 6	375	1E-103
	NP_006857	leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 2; leukocyte immunoglobulin-like receptor 7	375	1E-103
	NP_006831	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 5	371	1E-102
	AAM18038	leukocyte immunoglobulin-like receptor	359	2E-98
	AAM18036	leukocyte immunoglobulin-like receptor	358	2E-98
	AAC51885	immunoglobulin-like transcript 6	358	4E-98
	NP_006856	leukocyte immunoglobulin-like receptor, subfamily A (without TM domain), member 3;	358	4E-98
		leukocyte immunoglobulin-like receptor 4		

5

10

15

20

25



243

	AAM18040	leukocyte immunoglobulin-like receptor	357	8E-98
	AAM18041	leukocyte immunoglobulin-like receptor	357	8E-98
	AAM18035	leukocyte immunoglobulin-like receptor	356	1E-97
	AAM18037	leukocyte immunoglobulin-like receptor	356	1E-97
	AH28208	leukocyte immunoglobulin-like receptor, subfamily A (without TM domain), member 3	356	1E-97
	AB87661	leukocyte immunoglobulin-like receptor-4; LIR-4	355	3E-97
	AB68667	monocyte inhibitory receptor precursor	353	7E-97
	AH36827	Unknown (protein for MGC46153)	352	2E-96
	NP_005865	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 2;	352	2E-96
		leukocyte immunoglobulin-like receptor 2		
	AAL36990	leukocyte immunoglobulin-like receptor-2	352	2E-96
	AACS1883	immunoglobulin-like transcript 4	352	2E-96
	AACS1880	immunoglobulin-like transcript 2b	351	4E-96
	AAL36991	leukocyte immunoglobulin-like receptor-2	350	6E-96
	AB88119	immunoglobulin-like transcript 4; IL74	350	8E-96
	AB67711	MIR-10	350	8E-96
	NP_006660	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1;	349	1E-95
		leukocyte immunoglobulin-like receptor 1; CD85 antigen		
	AACS1879	immunoglobulin-like transcript 2a	345	2E-94
	AG08984	leukocyte immunoglobulin-like receptor 1	345	2E-94
	AB63522	leukocyte immunoglobulin-like receptor-1	345	2E-94
	AACS1881	immunoglobulin-like transcript 2c	345	2E-94
	AAL36989	leukocyte immunoglobulin-like receptor-1	345	2E-94
	AB67710	MIR-7	345	2E-94
	AAL36988	leukocyte immunoglobulin-like receptor-1	345	2E-94
	XP_115639	similar to immunoglobulin-like transcript 8	271	6E-72
	NP_077293	leukocyte immunoglobulin-like receptor, subfamily A, member 5; immunoglobulin-like transcript 10	260	8E-69
		immunoglobulin-like transcript 10 protein	258	5E-68

5

10

15

20

25

244

			BAC03380	FLJ00275 protein	241	4E-03
			BAB71361	unnamed protein product	241	6E-03
			AAC51886	immunoglobulin-like transcript 6a	218	6E-56
NM_019922	Mm.20904	F.2.03 (11to19)	AAH08745.1	cartilage associated protein	666	0
NP_064306.1			NP_006362.1	cartilage associated protein; cartilage-associated protein	666	0
			BAC03743.1	unnamed protein product	633	1E-180
			CAC16786.1	nucleolar protein No55	403	1E-111
			NP_006446.1	nucleolar autoantigen (53kD) similar to rat synaptonemal complex	402	1E-111
A.F.3.8.5.6.8.2	Mm.27242	F.2.03 (7to11)	NP_071442.1	EGF-TN7-larophilin-related protein	934	0
AAK62363.1			BAA34488.1	KIAA0768 protein	359	2E-98
			NP_056051.1	lectomedin-3	348	4E-95
			AAD54676.1	lectomedin-1 beta	341	4E-93
			NP_036134.1	larophilin 1; KIAA0786 protein; lectomedin-1; larophilin	341	4E-93
			AAD54675.1	lectomedin-1 alpha	341	4E-93
			BAA34506.1	KIAA0786 protein	337	8E-92
			AAG27461.1	lectomedin-2	330	1E-89
			NP_055736.1	lectomedin-2; KIAA0821 protein	330	1E-89
			AAH07587.1	Unknown (protein for IMAGE3162852)	322	2E-87

5

10

15

20

245

		NP_690880.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform b	281	4E-75
		NP_001775.2	CD97 antigen, isoform 2 precursor; leukocyte antigen CD97; seven-span transmembrane protein	280	2E-74
		NP_115960.1	egf-like module-containing mucin-like receptor 3 isoform a	278	5E-74
		AAF21974.1	EGF-like module EMR2	277	8E-74
		NP_038475.2	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform a	275	4E-73
		BAC06146.1	seven transmembrane helix receptor	275	4E-73
		B3725	leucocyte antigen CD97	275	5E-73
		NP_510966.1	CD97 antigen, isoform 1 precursor; leukocyte antigen CD97; seven-span transmembrane protein	265	3E-70
		AA336682.1	CD97	265	3E-70
		BAC06178.1	seven transmembrane helix receptor	265	3E-70
		BAC06133.1	seven transmembrane helix receptor	260	1E-68
		P48960	Leucocyte antigen CD97 precursor	260	1E-68
		NP_001965.1	egf-like module containing, mucin-like, hormone receptor-like sequence 1; egf-like module containing, mucin-like, hormone receptor-like	259	2E-68
		NP_690881.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform c	254	7E-67
		NP_690883.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform e	231	6E-60
		NP_690882.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform d	231	6E-60
		NP_690885.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform g	231	6E-60
		NP_690884.1	egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform f	231	6E-60
		AA05172.1	R29368_2	225	4E-58
		NP_002429.1	mannose receptor C type 1 precursor; mannose receptor precursor; macrophage mannose receptor	2521	0
		NP_006030.1	mannose receptor, C type 2; KIAA0709 gene product; endocytic receptor (macrophage mannose receptor family); likely ortholog of mouse mannose receptor, C type 2	831	0

5

10

15

20

246

				AA030280.1	endocytic receptor Endo180	830	0
				NP_031392.2	phospholipase A2 receptor 1, 180kDa; phospholipase A2 receptor 1, 180kD	573	1E-162
5				NP_002849.1	ATP-binding cassette, sub-family D, member 3; Peroxisomal membrane protein-1 (70kD);	1214	0
				NP_033017.1	peroxisomal membrane protein 1 (70kD, Zellweger syndrome); peroxisomal membrane protein-1		
				S20313	peroxisomal membrane protein, 70K	1207	0
				CAA38470.1	70kD peroxisomal integral membrane protein	1155	0
				NP_000024.2	ATP-binding cassette, sub-family D (ALD), member 1; adrenoleukodystrophy protein	445	1E-124
				JC5712	adrenoleukodystrophy related protein	444	1E-124
10				1908394A	adrenoleukodystrophy protein	443	1E-124
				P33897	Adrenoleukodystrophy protein (ALDP)	443	1E-124
				NP_005155.1	ATP-binding cassette, sub-family D, member 2; adrenoleukodystrophy-like 1; hALDR	442	1E-124
15				NP_055695.1	KTAA0022 gene product	251	2E-66
				NP_009207.2	chromobox homolog 3; heterochromatin protein HP1 gamma, HP1 gamma homolog,	261	2E-69
				NP_031650.1	heterochromatin-like protein 1		
				AAF62370.1	heterochromatin-like protein 1	261	3E-69
20				Q13185	Chromobox protein homolog 3 (Heterochromatin protein 1 homolog gamma) (HP1 gamma)	259	1E-68
					(Modifier 2 protein) (HECH)		
				AA048101.1	HP1 gamma	259	1E-68
				NP_006798.1	chromobox homolog 1 (HP1 beta homolog Drosophila); heterochromatin protein p25 beta,	199	1E-50
					chromobox homolog 1 (Drosophila HP1 beta)		
25				NP_000958.1	ribosomal protein L3; 60S ribosomal protein L3; HIV-1 TAR RNA-binding protein B	783	0

247

				AAH08492.1	ribosomal protein L3	780	0
				184501	ribosomal protein L3 - human (fragment)	773	0
				AAH22790.1	Unknown (protein for IMAGE:3538792)	724	0
				CAB76201.1	ribosomal protein L3	662	0
				NP_005052.1	ribosomal protein L3-like; 60S ribosomal protein L3-like	636	0
				AAK61301.1	60S ribosomal protein L3 like	634	0
				XP_172501.1	similar to ribosomal protein L3; 60S ribosomal protein L3; HIV-1 TAR RNA-binding protein B	625	1E-179
				AA91344.1	AREP-b gene product	532	1E-151
				AAH04323.1	Similar to RIKEN cDNA 1110057H16 gene	448	1E-126
				XP_070263.1	similar to ribosomal protein L3; 60S ribosomal protein L3; HIV-1 TAR RNA-binding protein B	419	1E-117
				NP_003387.1	tyrosylprotein sulfortransferase 1	734	0
				NP_003386.1	tyrosylprotein sulfortransferase 2; Tyrosylprotein phosphotransferase 2	486	1E-137
				CAB66558.1	hypothetical protein	481	1E-135
				XP_092649.1	similar to Kupffer cell receptor	509	1E-144
				BAC04786.1	unnamed protein product	433	1E-121
				NP_056532.1	Langerhans cell specific c-type lectin; langerin	168	3E-41
				NP_005470	frequently rearranged in advanced T-cell lymphomas	312	2E-84

5

10

15

20

Accession	Gene	Protein	Function	Interactions	References
BAAB8632		GSK-3beta binding protein FRAT1			310 8E-84
AAH34476		frequently rearranged in advanced T-cell lymphomas			308 3E-83
NM_008905	Mm.2817	F2.02 (7to19)	hypothetical protein		1462 0
NP_032931.1			similar to protein tyrosine phosphatase, receptor-type, F interacting protein, binding protein 2		1455 0
			similar to hypothetical protein		1453 0
			liprin-beta2		1299 0
			PTPRF interacting protein, binding protein 1 (liprin beta 1)		742 0
			KIAA1230 protein		663 0
NM_030693	Mm.1566	F2.02 (7to19)	activating transcription factor 5		177 5E-44
NP_09618.1			activating transcription factor 5		164 3E-40
NM_008280	Mm.362	F2.02 (5to19)	lipase C precursor		780 0
NP_032306.1			hepatic lipase precursor		778 0
			triacylglycerol lipase (EC 3.1.1.3) precursor, hepatic		777 0
			endothelial lipase precursor, endothelial cell-derived lipase		415 1E-114
			lipoprotein lipase precursor		396 1E-109
			Similar to lipoprotein lipase		393 1E-109
			lipoprotein lipase precursor		311 2E-83

249

NM_008407	Mm.4517	F:2.02 (5o19)	NP_002208.1	pre-alpha (globulin) inhibitor, H3 polypeptide; Inter-alpha (globulin) inhibitor, H3 polypeptide	1471	0
NP_032433.1			S30350	inter-alpha-trypsin inhibitor heavy chain 3 precursor	1471	0
			P19827	Inter-alpha-trypsin inhibitor heavy chain H1 precursor (ITI heavy chain H1) (Inter-alpha-inhibitor heavy chain 1) (Inter-alpha-trypsin inhibitor complex component III) (Serum-derived hyaluronan-associated protein) (SHAP)	911	0
			S24391	inter-alpha-trypsin inhibitor heavy chain H1 precursor	908	0
			NP_002206.1	inter-alpha (globulin) inhibitor, H1 polypeptide	907	0
			S04484	inter-alpha-trypsin inhibitor chain 3 - human	878	0
			CAA32821.1	lambda HuITI-13	878	0
			CAA34346.1	inter-alpha-trypsin inhibitor C-terminal	872	0
			P19823	Inter-alpha-trypsin inhibitor heavy chain H2 precursor (ITI heavy chain H2) (Inter-alpha-inhibitor heavy chain 2) (Inter-alpha-trypsin inhibitor complex component II) (Serum-derived hyaluronan-associated protein) (SHAP)	669	0
			NP_002207.1	inter-alpha (globulin) inhibitor, H2 polypeptide	664	0
			Q14624	Inter-alpha-trypsin inhibitor heavy chain H4 precursor (ITI heavy chain H4) (Inter-alpha-inhibitor heavy chain 4) (Inter-alpha-trypsin inhibitor family heavy chain-related protein) (IHRP) (Plasma kallikrein sensitive glycoprotein 120) (PK-120) (GPI20) (PRO1831) [Contains: GP57]	602	1E-170
			AAD05198.1	inter-alpha-trypsin inhibitor family heavy chain-related protein	601	1E-170
			BAA07536.1	PK-120 precursor	601	1E-170
			NP_002209.1	inter-alpha (globulin) inhibitor H4 (plasma kallikrein-sensitive glycoprotein), inter-alpha (globulin) inhibitor, H polypeptide-like 1; inter-alpha (globulin) inhibitor, H4 polypeptide	601	1E-170
NM_009254	Mm.2623	F:2.02 (5o19)	NP_004559.2	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	549	1E-156
NP_032380.1						

5

10

15

250

	A48681	placental thrombin inhibitor	548	1E-156
	NP_002631.1	ne (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8	459	1E-129
	NP_004146.1	(ovalbumin type) serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9	445	1E-125
	NP_109591.1	(ovalbumin type) e (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	330	3E-90
	XP_036951.4	similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin	327	2E-89
	I38202	leupin precursor - human	327	2E-89
	I38201	squamous cell carcinoma antigen 1 - human	325	7E-89
	NP_008850.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3; squamous cell carcinoma antigen 1	325	9E-89
	IT0966	squamous cell carcinoma antigen	325	9E-89
	pd9j1JRR	Chain A, Human Plasminogen Activator Inhibitor-2.[loop (66-98) Deletionmutant] Complexed With Peptide Mimicking The Reactive Center Loop	317	2E-86
	AAH34528.1	Similar to serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8	313	3E-85
	NP_002566.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2; plasminogen activator inhibitor, type II (agutite-sepin)	306	6E-83
	NP_003015.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bornapin)	304	2E-82
	BAB40773.1	SCCA2b	303	3E-82
	AAH12609.1	Similar to serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2	303	5E-82
	AAA36413.1	plasminogen activator inhibitor	301	1E-81
	JC7118	leupin serine proteinase inhibitor	285	8E-77
	CAA04937.1	leupin	285	8E-77
NM_009658	Mm451	aldo-keto reductase family 1, member B1; aldehyde reductase 1; aldose reductase; low Km aldose	542	1E-154

5

10

15

20



251

NP_033788.1				reductase; Lij5-2 CTCL tumor antigen		
	AAA51714.1			aldose reductase	541	1E-154
	pdb2ACQ			Chain , Aldose Reductase (E.C.1.1.1.21) Wild Type Complexed With Nadpr And Glucose-6-Phosphate	540	1E-153
	pdb2ACU			Chain , Aldose Reductase (E.C.1.1.1.21) Mutant With Tyr 48 Replaced By His (Y48H) Complexed With Nadpr And Citrate	538	1E-153
	AAH05387.1			aldo-keto reductase family 1, member B1 (aldose reductase)	537	1E-152
	pdb1JABN			Chain , Aldose Reductase (E.C.1.1.1.21) Mutant With Cys 298 Replaced By Ser (C298S) Complex With Nauph	536	1E-152
	pdb1JAZ1			Chain , Abretatin Bound To C298aW219Y MUTANT HUMAN ALDOSE REDUCTASE	533	1E-151
	AAC36465.1			aldo-keto reductase	449	1E-126
	NP_064695.2			aldo-keto reductase family 1, member B10; aldose reductase-like 1; ald-keto reductase family 1, member B11 (aldose reductase-like); aldose reductase-like peptide; aldose reductase-related protein; small intestine reductase	448	1E-126
	XP_064099.2			similar to Aldose reductase (AR) (Aldehyde reductase)	397	1E-110
	XP_069833.1			similar to aldo-keto reductase family 1, member B10 (aldose reductase); aldose reductase-like 1; aldo-keto reductase family 1, member B11 (aldose reductase-like)	388	1E-108
	AAK58523.1			aldo-keto reductase family 1, member B11 (aldose reductase-like)	333	4E-91
	XP_089193.4			aldo-keto reductase loopADR	332	1E-90
	NP_113624.1			aldose reductase	318	1E-86
	XP_166652.1			aldo-keto reductase loopADR; aldo-keto reductase related protein	310	4E-84
	pdb2ALR			Chain , Aldehyde Reductase	297	3E-80
	NP_066057.1			aldo-keto reductase family 1, member A1; aldehyde reductase; alcohol dehydrogenase	297	3E-80
	NP_005980.1			aldo-keto reductase family 1, member D1; steroid-5-beta-reductase, beta polypeptide 1 (3-oxo-5-beta-steroid delta 4-dehydrogenase beta 1); steroid 5-beta-reductase	293	5E-79
	I403439A			aldehyde reductase	291	2E-78

252

			BAA99542.1	3-alpha-hydroxysteroid dehydrogenase variant	287	3E-77
			AAH20744.1	aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4)	286	4E-77
			NP_001800.1	aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4); chlordecone reductase; type I 3-alpha-HSD; Chlordecone reductase	286	4E-77
			BAA05122.1	3 alpha-hydroxysteroid/dihydrodiol dehydrogenase DD4	286	4E-77
			NP_001344.2	aldo-keto reductase family 1, member C1; dihydrodiol dehydrogenase 1; dihydrodiol dehydrogenase isoform DD1; type II 3-alpha-hydroxysteroid dehydrogenase; trans-1,2-dihydrobenzene-1,2-diol dehydrogenase; chlordecone reductase homolog; 20 alpha-hydroxysteroid dehydrogenase; aldo-keto reductase C; hepatic dihydrodiol dehydrogenase	283	5E-76
			AAA35658.1	chlordecone reductase	280	4E-75
NM_013484	Mm.2081		NP_000054.2	complement component 2 precursor, C3/C5 convertase	1136	0
NP_038312.1			C2HU	complement C2 precursor [validated]	1134	0
			BAB63292.1	C2	873	0
			NP_001701.1	complement factor B preproprotein; B-factor, properdin, C3 proactivator, C3 proaccelerator; glycine-rich beta-glycoprotein; C3/C5 convertase	495	1E-139
			P00751	Complement factor B precursor (C3/C5 convertase) (Properdin factor B) (Glycine-rich beta glycoprotein) (GBG) (PHF2)	495	1E-139
			AAH04143.1	B-factor, properdin	495	1E-139
			AAA36225.2	MHC serum complement factor B	427	1E-119
			AAH29781.1	Similar to complement component 2	412	1E-114

5

10

15

253

			AAK30167.1	factor D		349	1E-95
			NP_612382.1	hypothetical protein BC013995		377	1E-104
			BAB71502.1	unnamed protein product		269	2E-97
			XP_065813.2	similar to hypothetical protein BC013995		265	2E-96
			BAC04265.1	unnamed protein product		341	3E-93
			NP_036323.1	putative tumor suppressor FUS2		310	3E-84
			NP_056511	glutathione peroxidase 6		317	2E-86
			BAB85019	unnamed protein product		200	2E-51
			AAH00736.1	mannosidase, alpha, class 2B, member 1		1511	0
			NP_000519.1	mannosidase, alpha, class 2B, member 1; mannosidase, alpha B, lysosomal		1509	0
			AAC34130.1	lysosomal alpha-mannosidase		1507	0
			AAB03816.1	alpha-mannosidase		1499	0
			AAC50812.1	lysosomal acid alpha-mannosidase		1498	0
			JC2200	alpha-mannosidase (EC 3.2.1.24) precursor		1327	0
			AAC50811.1	truncated lysosomal acid alpha-mannosidase		516	1E-146
			XP_052620.6	flar to Epididymis-specific alpha-mannosidase precursor (Mannosidase alpha class 2B member		295	3E-79

5

10

15

20

254

234	2)	Epididymis-specific alpha-mannosidase precursor (Mannosidase alpha class 2B number 2)	294	6E-79
Q9Y2E5	NP_036370.2	siroin 1; siroin (silent mating type information regulation 2, <i>S. cerevisiae</i> , homolog) 1; siroin type 1; sir2-like 1; SIR2alpha	1032	0
NP_062786.1	CAC04174.1	ba57G10.4 (SIRT1, Sir2-like proteins (siroins) type 1)	934	0
AAH12499.1	AAH12499.1	Unknown (protein for MGC:21066)	928	0
NP_055764.1	NP_055764.1	KIAA0907 protein	752	0
AAH27182.1	AAH27182.1	Similar to KIAA0907 protein	319	2E-85
AAH09503.1	AAH09503.1	G1 to S phase transition 1	872	0
NP_002085.1	NP_002085.1	G1 to S phase transition 1	868	0
CAB91089.1	CAB91089.1	polypeptide chain release factor 3b	861	0
NP_060564.1	NP_060564.1	peptide chain release factor 3	860	0
AAH36077.1	AAH36077.1	G1 to S phase transition 2	855	0
BAB14455.1	BAB14455.1	unnamed protein product	796	0
XP_017821.2	XP_017821.2	similar to peptide chain release factor 3	354	2E-96
BAA82990.1	BAA82990.1	KIAA1038 protein	316	7E-85

25

30

35

40

255

				NP_006611.1	HBS1-like	316	7E-85
A K 0 0 3 2 3 7	Mm.29703			NP_076869.1	hypothetical protein IMAGE3455200	216	3E-55
BA822661.1							
NM_008124	Mm.21198			NP_000157.1	gap junction protein, beta 1, 32kDa (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked); Gap junction protein, beta 1, 32kD (connexin 32); gap junction protein, beta 1, 32kD (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked)	551	1E-155
NP_032150.2				AA091440.1	gap junction protein beta 2	320	4E-86
				NP_003995.1	gap junction protein, beta 2, 26kDa (connexin 26); gap junction protein, beta 2, 26kD (connexin 26)	318	1E-85
				NP_006774.1	gap junction protein, beta 6 (connexin 30)	313	3E-84
				XP_060532.1	similar to Gap junction beta-4 protein (Connexin 30.3) (Cx30.3)	257	3E-67
				NP_005259.1	gap junction protein, beta 5 (connexin 31.1)	251	2E-65
				AAC95472.1	connexin 31.1	249	9E-65
				NP_076872.1	gap junction protein, beta 3, 31kDa (connexin 31); gap junction protein, beta 3, 31kD (connexin 31)	248	2E-64
				CAC93845.1	connexin25	227	4E-58
				P48165	Gap junction alpha-8 protein (Connexin 50) (Cx50) [Lens fiber protein MP70]	216	5E-55
				XP_088689.1	similar to Gap junction beta-1 protein (Connexin 32) (Cx32) (GAP junction 28 kDa liver protein)	216	5E-55
				NP_005258.1	gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8 (connexin 50); gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)	215	1E-54
				NP_068773.2	gap junction protein, alpha 3, 40kDa (connexin 46); gap junction protein, alpha 3, 40kD (connexin 46)	213	4E-54

256

			Q9Y6H8	Gap junction alpha-2 protein (Connexin 46) (Cx46)		213	4E-54
			NP_000156.1	connexin-43; gap junction protein, alpha 1, 43kD (connexin 43); gap junction protein, alpha 1, 43kD		203	6E-51
			NP_008924.1	nucleophosmin/nucleoplasmin 3; nucleoplasmin-3; nucleophosmin/nucleoplasmin family, member 3		234	2E-61
			AAD31496.1	nucleophosmin/nucleoplasmin3		224	1E-58
			XP_030699.1	similar to Cathepsin Z precursor (Cathepsin X) (Cathepsin P)		539	1E-153
			AAC39839.1	cathepsin Z precursor; CTSZ		539	1E-153
			AAC63141.1	preprocathepsin P		539	1E-153
			pd01IDEU	Chain A, Crystal Structure Of Human Procathepsin X: A Cysteine Protease With The Proregion Covalently Linked To The Active Site Cysteine		536	1E-152
			AAC61477.1	cathepsin X precursor		534	1E-151
			pd01EF7	Chain A, Crystal Structure Of Human Cathepsin X		474	1E-133
			NP_002970.2	sterol carrier protein 2		390	1E-107
			AAA03558.1	sterol carrier protein-2		390	1E-107
			AAB41286.1	sterol carrier protein-X/sterol carrier protein-2		387	1E-107
			B00407	sterol carrier protein 2-related form, 58.85k		378	1E-104
			AAA03559.1	sterol carrier protein-2		245	4E-64
			AAB24921.1	sterol carrier protein 2; SCP2		236	2E-61
			pd01QND	Chain A, Sterol Carrier Protein-2, Ntm, 20 Structures		208	7E-53

5

10

15

20

257

NM_008331	Mm.6718	F2 (5to19)	AAH07091	Unknown (protein for MGC:14710)	456	1E-127
NP_032357.1			NP_001539.1	interferon-induced protein with tetratricopeptide repeats 1; Interferon, alpha-inducible protein (MW 56kD); interferon-induced protein 56	455	1E-126
			NP_036552.1	retinoic acid- and interferon-inducible protein (58kD)	395	1E-108
			XP_084477.1	similar to Interferon-induced protein with tetratricopeptide repeats 2 (IFI-2) (Interferon-induced 54 kDa protein) (IFI-54K) (ISG-54 K)	295	1E-78
			AAH32839.1	Similar to interferon-induced protein with tetratricopeptide repeats 2	274	3E-72
			NP_001540.1	interferon-induced protein with tetratricopeptide repeats 4	272	2E-71
			XP_048183.1	similar to Interferon-induced protein with tetratricopeptide repeats 4 (IFI-4) (Interferon-induced 60 kDa protein) (IFI-60K) (ISG-60) (CIG49) (Retinoic acid-induced gene G protein) (RIG-G)	271	3E-71
			AAH04977.1	interferon-induced protein with tetratricopeptide repeats 4	268	2E-70

258

Table 1B: Unfavorable Genes/Proteins

Mouse Gene Protein	Unigene	Behavior	Human Proteins	Description	Bits	E
NM_007702 NP_031728.1	Mm.449	U:52.77 (YtoO)	AAC34987.1	cell death activator CIDE-A	340	3E-92
			AAH31896.1	Similar to cell death-inducing DFFA-like effector a	319	5E-86
NM_007822 NP_031848.1	Mm.7459	U:18.8 (5io7)	NP_000769.1	cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-	780	0
			Q02928	omega-alkane-1 monooxygenase; lauric acid omega-hydroxylase	777	0
			I65981	Cytochrome P450 4A11 precursor (CYP4A11) (Fatty acid omega-hydroxylase) (P-450 HK- omega) (Lauric acid omega-hydroxylase) (CYP4A11) (P450-HL-omega) fatty acid omega-hydroxylase (EC 1.14.13.-) cytochrome P450 4A11 AAB80170, Sequence 6 from patent US 5667992 fatty acid omega-hydroxylase	765	0
			BAA02864.1		761	0
			AAF76722.1	fatty acid omega-hydroxylase CYP4A11	746	0
			CAB72103.1	dJ18D14.4 (cytochrome P450, subfamily IVA, polypeptide 11)	736	0
			O4HUB1	O4HUB1 cytochrome P450 4B1	499	1E-139
			AAL57720.1	NP_305847 Cytochrome P450 family member (57.2 kD) [Caenorhabditis elegans]	499	1E-139
			AAM09532.1	cytochrome P450	499	1E-139
			NP_000770.1	cytochrome P450, subfamily IVB, polypeptide 1; cytochrome P450, subfamily IVB, member 1; mitochondrial monooxygenase	497	1E-139
			AAL57721.1	cytochrome P450	497	1E-139
			AAH17758.1	Unknown (protein for MGC:22150)	495	1E-138
			AAH28102.1	Unknown (protein for MGC:40051)	489	1E-137

5

10

15

20



259

			BAC03751.1	unnamed protein product	448	1E-124
			BA_C04868.1	unnamed protein product	402	1E-110
			BAA75823.1	Leukotriene B4 omega-hydroxylase	398	1E-109
			NP_0010773.3	cytochrome P450, subfamily IVF, polypeptide 2, leukotriene B4 omega-hydroxylase; leukotriene-B4 20-monoxygenase	398	1E-109
			NP_000887.1	cytochrome P450, subfamily IVF, polypeptide 3; leukotriene B4 omega hydroxylase; leukotriene-B4 20-monoxygenase; cytochrome P450-LTB-omega	394	1E-108
			AA_C50052.2	cytochrome P450 4F2	393	1E-108
			AAC08589.1	cytochrome P-450	390	1E-107
			Q9HB16	Cytochrome P450 4F11 (CYP11B1)	387	1E-106
			NP_067010.1	cytochrome P450, subfamily IVF, polypeptide 11	387	1E-106
			Q9HCS2	Cytochrome P450 4F12 (CYP11B2)	384	1E-105
			NP_076433.1	cytochrome P450 isoform 4F12	384	1E-105
			AAH35350.1	similar to cytochrome P450	384	1E-105
			AAC11543.1	P2329_1	381	1E-104
			NP_009184.1	cytochrome P450, subfamily IVF, polypeptide 8; microsomal monoxygenase, flavoprotein-linked monoxygenase	380	1E-104
			CAD38795.1	hypothetical protein	347	6E-94
			XP_065069.2	record was removed	337	6E-91
			XP_029070.2	record was removed	323	9E-87
			AAH2851.1	(Similar to cytochrome P450, subfamily IVa, polypeptide 11	287	6E-76
			XP_065068.1	record was removed	278	2E-73
			BAC05026.1	unnamed protein product	278	2E-73
			BAA02145.1	cytochrome P-450L7BV	270	6E-71
			CAA50586.1	cytochrome P450	263	1E-68
			AAH57719.1	truncated cytochrome P450	237	5E-61
			AAH77876	protein tyrosine kinase non catalytic form	868	0
			U:14.81 (Y100)			
			NP_032771.1	neurotrophin receptor tyrosine kinase type 2	846	0

5

10

15

20

25





252

			AA053409	OSBP-related protein 6; ORP6		914	0
			NP_665682	oxysterol-binding protein-like protein 6 isoform b; oxysterol-binding protein-related protein 6; OSBP-related protein 6		895	0
			BA004248	unnamed protein product		894	0
			NP_663164	oxysterol-binding protein-like protein 3 isoform f; oxysterol-binding protein-related protein 3; OSBP-related protein 3		858	0
			NP_663163	oxysterol-binding protein 3; OSBP-related protein 3		842	0
			BA055223	oxysterol-binding protein-like protein 3 isoform e; oxysterol-binding protein-related protein 3; OSBP-related protein 3		733	0
			AAG53410	unnamed protein product		733	0
			AAL06659	OSBP-related protein 7; ORP7		721	0
			AAB83939	oxysterol-binding protein-like protein OSBP.L7		423	1E-117
			AAG53408	OXYSTEROL-BINDING PROTEIN; 45% similarity to P22059		396	1E-109
			AAM74166	OSBP-related protein 3; ORP3		386	1E-105
			AAM74165	oxysterol binding protein-related protein 3 isoform 2d		370	1E-101
			BA091043	oxysterol binding protein-related protein 3 isoform 2c		306	2E-81
			AAC26985	unnamed protein product		299	2E-79
			NP_542164	match to EST AA376471 (NID:G2028790)		269	2E-70
				oxysterol-binding protein-like 1A isoform B; oxysterol-binding protein-related protein 1; oxysterol-binding protein-like 1B; OSBP-related protein 1		269	2E-70
			AAL00663	oxysterol-binding protein-like protein OSBP.L1B		269	2E-70
			AAL00662	oxysterol-binding protein-like protein OSBP.L1A		269	2E-70
			AAK15154	oxysterol-binding protein-related protein		263	9E-69
			CAC22307	bA157P1.3.1 (KIAA0772, isoform 1)		263	9E-69
			AAL00660	oxysterol-binding protein-like protein OSBP.L2		261	2E-70
			AAH11581	Similar to oxysterol binding protein		246	2E-63
			BAB33334	KIAA1664 protein		246	2E-63
			Q969R2	Oxysterol-binding protein 2 (Oxysterol binding protein-related protein 4) (OSBP-related protein 4) (ORP-4)		246	2E-63
			AAG53406	OSBP-related protein 4		246	2E-63

5

10

15

20

263

				unnamed protein product	BAC04091				246	2E-63
				OXYSTEROL-BINDING PROTEIN-like; similar to P22059 (PID:g129308)	AAC12953				242	2E-70
				similar to oxysterol-binding proteins; 76% Similarity to P22059	AAC26986				241	2E-70
				oxysterol-binding protein-like 1A isoform C; oxysterol-binding protein-related protein 1;	NP_579802				222	2E-70
				oxysterol-binding protein-like 1B; OSBP-related protein 1						
				unnamed protein product	BAA91496				216	2E-70
				hypothetical protein F132191	NP_653290				325	1E-87
				zinc finger protein 25	NP_659448				323	7E-87
				unnamed protein product	BAB71272				313	7E-84
				KIAA1881 protein	BAB67774.1				1524	0
				similar to KIAA1881 protein	XP_170901.1				248	6E-64
				Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	P00746				370	1E-102
				adipsin/complement factor D precursor	CAC48304.1				358	4E-99
				precursor [validated] - human (fragment)	67580				352	5E-97
				Chain A, Proenzyme Of Human Complement Factor D, Recombinant Prefactor D	6730437				340	1E-93
				Chain, Mutant Of Factor D With Enhanced Catalytic Activity	1632327				330	1E-90
				Chain, Human Complement Factor D In Complex With Isoic Anhydride Inhibitor	5542120				329	3E-90
				similar to Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	XP_084037.1				328	8E-90
				adipsin/complement factor D precursor	NP_001919.1				324	1E-88
				glutathione S-transferase A1; GST, class alpha. 1; glutathione S-alkyltransferase A1; glutathione S-ary/transferase A1; S-(hydroxyalkyl)glutathione lyase A1; glutathione S-alkyltransferase A1;	NP_665083.1				328	8E-90

5

10

15

20

25

264

				GST-epsilon; glutathione S-transferase 2		
		152381		record was removed 152381-GI number 2473582 references a Nucleotide record; you are currently using the Protein database	327	1E-89
		DAA00071.1		TPA; glutathione transferase A5	327	1E-89
		442977		Chain A, Glutathione S-Transferase A1-1 (E.C.2.5.1.18)	326	3E-89
		1127144		Chain A, Glutathione Transferase A1-1 Complexed With An Ethacrynic Acid Glutathione Conjugate (Mutant R15k)	325	6E-89
		XP_167100.2		record was removed	325	6E-89
		Q16772		Glutathione S-transferase A3-3 (GST class-alpha)	324	1E-88
		NP_000338.2		record was removed	322	3E-88
		A49365		GI number 2302844 references a Nucleotide record; you are currently using the Protein database	322	4E-88
		AAA74634.1		glutathione S-transferase A3	322	4E-88
		S20331		record was removed	318	5E-87
		S27110		record was removed	317	1E-86
		S24330		glutathione transferase (EC 2.5.1.18) alpha-2 (clone GTH2)	316	3E-86
		NP_000837.2		glutathione S-transferase A2; glutathione S-transferase 2; GST, class alpha, 2; liver GST2; glutathione S-alkyltransferase A2; glutathione S-ryltransferase A2; S-(hydroxyalkyl)glutathione	315	4E-86
		CAB92770.1		lyase A2; glutathione S-alkyltransferase A2; GST-gamma; HA subunit 2		
		d15217.3		(glutathione S-transferase A2)	315	4E-86
		S77948		glutathione transferase (EC 2.5.1.18) alpha-2 (clone GTH2 (+))	309	3E-84
		A56001		record was removed A56001 GI number 3712816 references a Nucleotide record; you are currently using the Protein database.	309	4E-84
		CAA69685		Spot14 protein	221	3E-57
		NIM_009381		U:5.69 (YtoC)		
		NP_033407.1				
		Mm.75856		U:5.55 (YtoC)		
		AK016553		heat shock transcription factor 2 binding protein; heat shock factor 2 binding protein	549	1E-155
		BAB30300.1		heat shock transcription factor 2 binding protein	378	1E-103

30

35

40

45

265

U89406		U:5.43 (YtoO)	NP_004095	fatty acid synthase	270	9E-72
AAC36513.1			AAH07267	Unknown (protein for IMAGE:3138929)	270	9E-72
			G01880	fatty acid synthase (EC 2.3.1.85) (version 2)	267	4E-71
			A57788	enoyl-[acyl-carrier-protein] reductase (NADPH2, B-specific) (EC 1.3.1.10) (version 1)	234	3E-67
NM_025541	Mm.28606	U:5.13 (YtoM)	CAB43363	hypothetical protein	414	1E-114
NP_079817.1			AAF29110	HSPC146	412	1E-114
			CAC05410	d329J.24.2 (hypothetical 23.0 KD protein.)	339	6E-92
			AAK82973	anti-silencing function 1B	290	3E-77
			BAA91602	unnamed protein product	289	8E-77
A F 2 8 1 0 4 5	Mm.87471	U:4.86 (Sto11)	NP_066956.1	ribonuclease 1 (2',5'-oligoadenylate synthetase-dependent), ribonuclease 4	904	0
AAG33708.1			A45771	A45771	900	0
A K 0 0 6 0 9 6	Mm.38305	U:4.75 (YtoO)	AAH11587	Similar to RIKEN cDNA 1700018O18 gene	779	0
BAB24407.1			BAC04100	unnamed protein product	770	0
			AAH06353	Similar to RIKEN cDNA 1700018O18 gene	550	1E-155
NM_008495	Mm.43831	U:4.6 (7to11)	NP_002296.1	beta-galactosidase binding lectin precursor; Lectin, galactose-binding, soluble, 1;	259	2E-69
NP_032521.1			1713410A	beta galactoside soluble lectin	257	6E-69
NM_025429	Mm.46316	U:4.44 (5to19)	NP_109391.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	498	1E-140
NP_079705.1						

5

10

15

20

25

266

			NP_004146.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)	276	6E-74
			NP_005015.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bonapin)	275	1E-73
			NP_002631.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)	275	2E-73
			NP_004559.2	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	272	1E-72
			A48681	placental thrombin inhibitor - human	269	9E-72
			I38202	leupin precursor - human	267	3E-71
			XP_036951.4	similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	266	8E-71
			I5988197	Chain A, Human Plasminogen Activator Inhibitor-2, [loop (66-98) Deletionmutant] Complexed With Peptide Mimicking The Reactive Center Loop	265	2E-70
			2118383	squamous cell carcinoma antigen 1 - human	264	3E-70
A F 3 3 2 0 5 2	Mm.25316	U:4.08 (YtoO)	AAH06195	ATP citrate lyase	2101	0
AAK56081.1			AAB60340	ATP: citrate lyase.	2100	0
			CAA45614	ATP-citrate (pro-S)-lyase	2046	0
			BAC04484	unnamed protein product	1340	0
A K 0 1 8 2 2 6	Mm.92685	U:4.01 (5to19)	NP_109591.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	345	1E-138
XP_181363.1			NP_004146.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)	200	5E-79
			NP_002631.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)	207	2E-76



267

			NP_003015.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bomapin)	179	4E-75
			NP_004559.2	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	192	4E-75
			U3.91 (YtoO)	Chain A, Human Plasminogen Activator Inhibitor-2, [loop (66-98) Deletionmutant] Complexed With Peptide Mimicking The Reactive Center Loop	199	5E-75
			XP_097818	similar to Probable serine/threonine protein kinase SNF1LK	1172	0
			NP_775490	SNF1-like kinase	1171	0
			BAA95536	gene similar to rat protein Kinase (KID2)	1163	0
			BAA34501	KIAA0781 protein	572	1E-161
			XP_041314	similar to Probable serine/threonine protein kinase SNF1LK	572	1E-161
			BAB91442	KIAA0781 protein	512	1E-143
			BAA76843	KIAA0999 protein	412	1E-113
			AAH08771	Similar to ELK1 motif kinase	360	1E-97
			AAK82368	Ser/Thr protein kinase PAR-1Ba1pha	360	1E-97
			NP_004945	MAP/microtubule affinity-regulating kinase 2 isoform b; ELKL motif kinase 1; ELKL1 motif kinase	359	2E-97
			G01025	serine/threonine protein kinase	359	2E-97
			NP_059672	MAP/microtubule affinity-regulating kinase 2 isoform a; ELKL motif kinase 1; ELKL1 motif kinase	359	2E-97
			NP_061120	MAP/microtubule affinity-regulating kinase 1	357	1E-96
			AAC15093	Gla25C associated protein kinase C-TAK1	352	2E-95
			AAH24773	Unknown (protein for MGC:29880)	352	2E-95

5

10

15

268

		AAL23683	MARK4 serine/threonine protein kinase	332	2E-95
		AAK32367	Ser/Thr protein kinase PAR-1A	352	2E-95
		BAB47489	KIAA1860 protein	352	2E-95
		S27966	probable serine/threonine-specific protein kinase (EC 2.7.1.1.)	351	5E-95
		AAI69982	MAP/microtubule affinity-regulating kinase 3 long isoform	351	7E-95
		BAC03375	microtubule affinity-regulating kinase-like 1	349	2E-94
		NP_113005	MAP/microtubule affinity-regulating kinase like 1; MARK4 serine/threonine protein kinase	349	2E-94
		AAD48007	serine/threonine protein kinase Kp78 splice variant CTAK75a	339	3E-91
		AAK33487	R31237_1, partial CDS	335	3E-90
		BAA96001	KIAA1477 protein	321	6E-86
		BAA07744	KIAA0095 gene product is related to a protein kinase.	285	3E-75
		P54646	5'-AMP-activated protein kinase, catalytic alpha-2 chain (AMPK alpha-2 chain)	285	6E-75
		AAJ86944	HSNFRK	283	2E-74
		CAA75033	immunoglobulin lambda light chain	293	2E-78
		S25749	Ig lambda chain	276	2E-73
		BAC01857	immunoglobulin lambda light chain VLI region	268	4E-71
		BAC01837	immunoglobulin lambda light chain VLI region	268	5E-71
		BAC01863	immunoglobulin lambda light chain VLI region	268	5E-71
		BAC01842	immunoglobulin lambda light chain VLI region	268	7E-71
		BAC01808	immunoglobulin lambda light chain VLI region	265	6E-70
		BAC01859	immunoglobulin lambda light chain VLI region	264	8E-70

5

10

15

20

269

		BAC01813	immunoglobulin lambda light chain VLI region	263	2E-69
		BAC01822	immunoglobulin lambda light chain VLI region	263	2E-69
		BAC01812	immunoglobulin lambda light chain VLI region	263	2E-69
		BAC01823	immunoglobulin lambda light chain VLI region	263	2E-69
		BAC01834	immunoglobulin lambda light chain VLI region	262	3E-69
		BAC01838	immunoglobulin lambda light chain VLI region	262	3E-69
		BAC01820	immunoglobulin lambda light chain VLI region	262	3E-69
		BAC01821	immunoglobulin lambda light chain VLI region	262	3E-69
		BAC01840	immunoglobulin lambda light chain VLI region	262	4E-69
		1203309 A.	Ig lambda VI THO	261	5E-69
		BAC01824	immunoglobulin lambda light chain VLI region	261	6E-69
		BAC01846	immunoglobulin lambda light chain VLI region	261	6E-69
		BAC01841	immunoglobulin lambda light chain VLI region	260	1E-68
		BAC01844	immunoglobulin lambda light chain VLI region	260	1E-68
		BAC01862	immunoglobulin lambda light chain VLI region	260	1E-68
		A42193	Ig lambda chain (BJP-DJA)	260	1E-68
		BAC01799	immunoglobulin lambda light chain VLI region	260	1E-68
		BAC01860	immunoglobulin lambda light chain VLI region	260	1E-68
		BAC01797	immunoglobulin lambda light chain VLI region	259	2E-68
		BAC01814	immunoglobulin lambda light chain VLI region	259	2E-68
		BAC01810	immunoglobulin lambda light chain VLI region	259	3E-68
		BAC01778	immunoglobulin lambda light chain VLI region	259	3E-68
		BAC01792	immunoglobulin lambda light chain VLI region	259	3E-68
		BAC01828	immunoglobulin lambda light chain VLI region	259	3E-68
		BAC01847	immunoglobulin lambda light chain VLI region	258	4E-68
		AAH33102	Similar to immunoglobulin lambda joining 3	258	4E-68
		BAC01854	immunoglobulin lambda light chain VLI region	258	5E-68
		BAC01839	immunoglobulin lambda light chain VLI region	258	5E-68

5

10

15

20

25

270

			BAC01855	immunoglobulin lambda light chain VLJ region	258	7E-67
			BAC01833	immunoglobulin lambda light chain VLJ region	257	9E-68
			BAC01811	immunoglobulin lambda light chain VLJ region	257	1E-67
			S25744	Ig lambda chain	257	1E-67
			BAC01791	immunoglobulin lambda light chain VLJ region	257	1E-67
			S25738	Ig lambda chain	257	1E-67
			BAC01819	immunoglobulin lambda light chain VLJ region	256	2E-67
			BAC01786	immunoglobulin lambda light chain VLJ region	256	2E-67
			BAC01806	immunoglobulin lambda light chain VLJ region	256	2E-67
			BAC01831	immunoglobulin lambda light chain VLJ region	256	2E-67
			BAC01818	immunoglobulin lambda light chain VLJ region	256	2E-67
			BAC01779	immunoglobulin lambda light chain VLJ region	256	2E-67
			S25752	Ig lambda chain	256	2E-67
			1615309A	Ig lambda anti-Rh(c)	256	2E-67
			BAC01845	immunoglobulin lambda light chain VLJ region	256	3E-67
			BAC01782	immunoglobulin lambda light chain VLJ region	256	3E-67
			CAA40943	immunoglobulin lambda light chain	256	3E-67
			BAC01830	immunoglobulin lambda light chain VLJ region	256	3E-67
			BAC01852	immunoglobulin lambda light chain VLJ region	256	3E-67
			S06270	Ig lambda chain precursor	256	3E-67
			BAC01856	immunoglobulin lambda light chain VLJ region	255	4E-67
			BAC01787	immunoglobulin lambda light chain VLJ region	255	4E-67
			AAH30983	Similar to immunoglobulin lambda joining 3	255	4E-67
			S25746	Ig lambda chain	255	4E-67
			BAC01789	immunoglobulin lambda light chain VLJ region	255	4E-67
			BAC01832	immunoglobulin lambda light chain VLJ region	255	4E-67
			BAC01800	immunoglobulin lambda light chain VLJ region	255	5E-67
			S25757	Ig lambda chain - human	254	6E-67
			BAC01777	immunoglobulin lambda light chain VLJ region	254	6E-67

5

10

15

20

25

271

				immunoglobulin lambda light chain VLJ region	254	6E-67
				immunoglobulin lambda light chain VLJ region	254	6E-67
				immunoglobulin lambda light chain VLJ region	254	8E-67
				immunoglobulin lambda light chain VLJ region	254	8E-67
				immunoglobulin lambda light chain VLJ region	254	8E-67
				Ig lambda chain V region	254	8E-67
				immunoglobulin lambda light chain VLJ region	254	8E-67
				Chain A, Bence Jones Protein Cite. A Lambda Iii Immunoglobulin Light-Chain Dimer.	254	8E-67
				immunoglobulin lambda light chain VLJ region	254	8E-67
				similar to tropomyosin, fibroblast - human	691	0
				Glin derived nexin precursor (GDN) (Protease nexin I) (PN-I) (Protease inhibitor 7)	684	0
				glia-derived neurite promoting factor precursor	682	0
				Plasminogen activator inhibitor-1 precursor (PAI-1) (Endothelial plasminogen activator inhibitor)	310	4E-83
				(PAI)		
				plasmaogen activator inhibitor	310	6E-83
				Chain A, 1.8a Resolution Structure Of Latent Plasminogen Activator Inhibitor-(Pa-I)	310	6E-83
				NP_000593.1 serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1; plasminogen activator inhibitor, type I	310	6E-83
				prebeta-migrating plasminogen activator inhibitor	310	6E-83
				plasmaogen activator inhibitor 1	308	1E-82
				Plasminogen activator inhibitor-1 precursor (PAI-1) (Endothelial plasminogen activator inhibitor)	308	2E-82
				(PAI)		
				Plasminogen activator inhibitor-1 precursor (PAI-1) (Endothelial plasminogen activator inhibitor)	308	2E-82
				(PAI)		
				Plasminogen activator inhibitor-1 precursor (PAI-1) (Endothelial plasminogen activator inhibitor)	307	3E-82
				(PAI)		
				Chain A, Active Form Of Human Pai-1	305	2E-81

5

10

15

20

272

			CAA131208.1	PAI precursor polypeptide		305	2E-81
			NP_005016.1	ne (or cysteine) proteinase inhibitor, clade 1 (neuroserpin), member 1, protease inhibitor 12 (neuroserpin)		243	7E-63
			AAH18043.1	serine (or cysteine) proteinase inhibitor, clade 1 (neuroserpin), member 1		240	5E-62
			NP_006208.1	protease inhibitor 14; pancipin		219	1E-55
NM_021468	Mm.42188	U3.58 (MitoC)	NP_006368	UNC113 (C. elegans)-like; homolog of rat Munc13 (diacylglycerol-binding)		2958	0
NP_067443.1			BAA82984	KIAA1032 protein		1598	0
			XP_038604	similar to KIAA1032 protein		1478	0
			BAC03675	unnamed protein product		1404	0
			XP_085234	similar to Munc13-3 protein - rat		1328	0
			CAD39069	hypothetical protein		915	0
NM_007643	Mm.18628	U:3.57 (YtoC)	P16671	Platelet glycoprotein IV (GP1V) (GPIIIB) (CD36 antigen) (PAS IV) (PAS-4 protein)		798	0
NP_031669.1			NP_000063.1	CD36 antigen (collagen type I receptor, thrombospondin receptor); CD36 antigen (collagen type I)		796	0
			I59613	cell adhesion receptor CD36		791	0
			AAJ14636.1	CD36 antigen (collagen type I receptor, thrombospondin receptor)		780	0
			NP_005497.1	scavenger receptor class B, member 2; CD36 antigen (collagen type I receptor, thrombospondin receptor); CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 2 (lysosomal integral membrane protein II)		271	3E-72
			A56525	lysosomal integral membrane protein II		271	3E-72
			NP_005496.2	scavenger receptor class B, member 1; CD36 antigen-like 1; scavenger receptor class B type 1; CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 1		255	2E-67
			A48528	membrane glycoprotein CLA-1 protein long form precursor		252	2E-66
A K 0 0 7 2 9 3	Mm.159753	U:3.56 (5to11)	BAB67772.1	KIAA1879 protein		189	8E-47
BAB24937.1							

5

10

15

20

273

AK008016	Mm.27252	U3.37 (YtoO)	AAH21275	Similar to RIKEN cDNA 2010001M09 gene	266	3E-70
NM_013623	Mm.57239	U3.35 (Yto9)	NP_000598.1	orosomucoid 1 precursor; Orosomucoid-1 (alpha-1-acid glycoprotein-1), alpha-1-acid glycoprotein 1	165	3E-40
NP_038651.1			AAH26238.1	orosomucoid 1	165	4E-40
NM_020277	Mm.143747	U3.35 (Sto11)	NP_053370.1	transient receptor potential cation channel, subfamily M, member 5; MLSN1 and TRP-related; MLSN1- and TRP-related	1875	0
NP_064673.1			CAB66342.1	LTRPC5 protein	1875	0
			NP_060106.2	transient receptor potential cation channel, subfamily M, member 4	833	0
			AAI02142.1	TRP-related cation influx channel	728	0
			BAA90907.1	unnamed protein product	726	0
			BAA95563.1	transient receptor potential-related channel 7, a novel putative Ca2+ channel protein	696	0
			NP_002298.1	transient receptor potential cation channel, subfamily M, member 2; transient receptor potential-related channel 7, a novel putative Ca2+ channel protein; transient receptor potential channel 7	696	0
			CAD01139.1	putative TRP cation channel	688	0
			BAB86335.1	LTRPC6	510	1E-143
			NP_076985.3	transient receptor potential cation channel, subfamily M, member 8	510	1E-143
			NP_060132.2	transient receptor potential cation channel, subfamily M, member 6	398	1E-109
			AAK19738.2	channel-kinase 1	317	7E-85
			XP_030709.6	similar to LTRPC7	317	7E-85
			BAB15429.1	unnamed protein product	295	3E-78
			AAC80000.1	melastatin 1	270	1E-70

5

10

15

20

274

				NP_002411.2	transient receptor potential cation channel, subfamily M, member 1, melastatin 1	270	1E-70
NM_007809	Mm.1262	U3.21 (YtoM)		A26366	steroid 17alpha-monooxygenase (EC 1.14.99.9) cytochrome P450 17	710	0
NP_031835.1							
				AAA36405	cytochrome P450c17	709	0
				AAA52140	steroid 17alpha-hydroxylase	706	0
				CAA26458	cytochrome P(1)-450	248	2E-64
				Q4HU6	aryl hydrocarbon (benzo[a]pyrene) hydroxylase (EC 1.14.14.-) cytochrome P450 1A1	248	3E-64
				AAA52139	cytochrome P-450-1	246	1E-63
J00544	Mm.1192	U3.24 (YtoM)		NP_653247	immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	245	8E-64
AAA38673.1							
				AAA58902	Ig J-chain	228	1E-58
NM_031494	Mm.26595	U3.21 (YtoM)		Q9NSD4	Z275_HUMAN Zinc finger protein 275	840	0
NP_113682.1							
				BAC04309.1	unnamed protein product	363	2E-98
				P52742	Z135_HUMAN Zinc finger protein 135	360	2E-97
				CAD39111.1	hypothetical protein	357	2E-96
				AAF73235.1	AF24088_1 zinc finger protein	357	2E-96
				AAH10996.1	AAH10996 zinc finger protein 16 (KOX 9)	357	2E-96
				AAC50252.1	zinc finger protein ZNF132	357	2E-96
				AAH28377.1	hypothetical protein FLJ14855	349	4E-94
				AAH05868.1	Similar to zinc finger protein 304	348	5E-94
				NP_694563.1	hypothetical protein FLJ0726	347	2E-93
				NP_653290.2	hypothetical protein FLJ32191	346	2E-93
				AAH2863.1	Unknown (protein for MGC:33794)	346	2E-93
				BAC11133.1	unnamed protein product	343	2E-92
				NP_660355.1	Zinc finger protein 93 (Zinc finger protein HTF34)	343	2E-92
				XP_209899.1	similar to Zinc finger protein 184	343	3E-92

5

10

15

20

25



275

		AAA97578.1	ZNF157		342	3E-92
		BAB71272.1	unnamed protein product		342	4E-92
		NP_689817.1	hypothetical protein FLJ33863		342	4E-92
		AAC34327.1	F23269_2		342	4E-92
		CAC38160.1	bB479F17.1 (zinc finger protein 157 (HZF22))		342	4E-92
		XP_209140.1	similar to F23269_2		342	4E-92
		AAH42500.1	Similar to zinc finger protein 43 (HTF6)		342	4E-92
		AAH09433.1	zinc finger protein 331		341	7E-92
		AAH78075.1	KRAB zinc finger protein		341	7E-92
		NP_061121.1	zinc finger protein ZFP		340	1E-91
		BAB71257.1	unnamed protein product		340	1E-91
		AAH45649.1	Similar to hypothetical protein FLJ32191		340	1E-91
		CAC06610.1	zinc finger protein 304		340	2E-91
		BAB21801.1	KJAA1710 protein		339	3E-91
		AAH43151.1	Similar to zinc finger protein 208		339	3E-91
		Q9C0F3	Hypothetical zinc finger protein KJAA1710		339	3E-91
		XP_209718.1	similar to zinc finger protein 184 (Kruppel-like)		338	6E-91
		BAC04418.1	unnamed protein product		338	6E-91
		AAH28136.1	Similar to hypothetical protein MGC10520		338	8E-91
		AAH04480.1	Unknown (protein for MGC10520)		338	8E-91
		XP_087503.1	similar to zinc finger protein 91 (HPF7, HTF10)		338	8E-91
		BAC04610.1	unnamed protein product		337	1E-90
		XP_086070.1	similar to Zinc finger protein similar to Zinc finger protein 93 (Zinc finger protein HTF34)		337	1E-90
		P35789	ZNF93_HUMAN Zinc finger protein 93		337	1E-90
		NP_085116.1	hypothetical protein FLJ21628		337	2E-90
		XP_065116.3	similar to zinc finger protein 91 (HPF7, HTF10)		337	2E-90
		AAH33849.1	similar to Zinc finger protein 268 (Zinc finger protein HZF3)		336	3E-90
		BAB70771.1	unnamed protein product		336	3E-90
		CAD36551.1	hypothetical protein		335	4E-90

5

10

15

20

25

276

		AAK52068.1	ZNPPH133 protein	335	4E-90
		BAB15582.1	unnamed protein product	335	4E-90
		XP_032054.2	similar to zinc finger protein	335	5E-90
		BAB85542.1	KIAA1956 protein	335	5E-90
5		AAJ23607.1	AC007228_2 BC37295_	335	5E-90
		Q05481	ZN91_HUMAN Zinc finger protein 91 (Zinc	335	5E-90
		XP_083836.1	similar to Hypothetical zinc f	335	5E-90
		BAB71096.1	unnamed protein product	335	5E-90
		AAH08297.1	Similar to hypothetical protein	335	7E-90
		BAA92634.1	KIAA1396 protein	335	7E-90
10		XP_030378.2	similar to zinc finger protein 28; zinc finger factor X6	335	7E-90
		BAB47458.1	KIAA1829 protein	335	7E-90
		AAD39268.1	BC331191_1	334	9E-90
		NP_689690.1	hypothetical protein FLJ36991	334	9E-90
15		NP_035713.1	KIAA0961 protein	334	9E-90
		NP_055295.1	zinc finger protein AF020591	334	9E-90
		XP_209968.1	similar to DKFZF72C163 protein	334	1E-89
		XP_091895.5	similar to KIAA1947 protein	334	1E-89
		NP_150630.1	KRAB zinc finger protein KR18	334	1E-89
20		BAB13437.1	KIAA1611 protein	334	1E-89
		BAB85533.1	KIAA1947 protein	334	1E-89
		BAB15732.1	FLJ00032 protein	334	1E-89
		CAD38678.1	hypothetical protein	333	2E-89
		CAD36956.1	zinc finger protein 33b	333	2E-89
25		CAB45722.1	hypothetical protein	333	2E-89
		BAB14911.1	unnamed protein product	333	2E-89
		TI4757	hypothetical protein DKFZF72C163.1	333	3E-89
		NP_666016.1	zinc finger protein 23; zinc finger protein 32; zinc finger protein 359	333	3E-89
		BAB14145.1	unnamed protein product	333	3E-89

277

NM_008161	Mm.7156	U:3.13 (YtoO)		BAA00525.1	glutathione peroxidase	397	1E-109
NP_032187.2				JQ0476	glutathione peroxidase (EC 1.11.1.9) 3, precursor	397	1E-109
				AAH43005.1	extracellular glutathione peroxidase	390	1E-107
				CAA06463.1	glutathione peroxidase type 5 (GPX5)	301	1E-80
				BAA03864.1	plasma glutathione peroxidase	281	1E-74
				XP_167146.1	similar to EPIDIDYMAL SECRETORY GLUTATHIONE PEROXIDASE PRECURSOR (EPIDIDYMIS-SPECIFIC GLUTATHIONE PEROXIDASE-LIKE PROTEIN) (EGLP)	202	8E-51
NM_025724	Mm.56430	U:3.12 (MtoO)		NM_013559	Unknown (protein for MGC:26598)	262	2E-68
NP_080000.1				AAH24183	Similar to RIKEN cDNA 4921510H08 gene	262	2E-68
NM_011112.5	Mm.6105	U:3.1 (YtoO)		AAH19847.1	phospholipid transfer protein	744	0
NP_032255.1				NP_006218.1	phospholipid transfer protein	744	0
				CAC36020.1	gl337O18.1.2 (Phospholipid Transfer Protein II) (isoform 2))	634	0
				AAH05045.1	Similar to phospholipid transfer protein	633	0
NM_012006	Mm.1978	U:3.07 (Sto7)		XP_170752.1	similar to peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	602	1E-172
NP_036136.1				P49753	Peroxisomal acyl-coenzyme A thioester hydrolase 2a (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	600	1E-171
				AAH06500.1	Unknown (protein for MGC:2366)	600	1E-171
				NP_006812.2	peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	599	1E-171
				BAA91989.1	unmaned protein product	598	1E-171

5

10

15

20

278

				NP_689544.1	hypothetical protein [L31235	494	1E-139
				AAC42007.1	ORF, putative	405	1E-113
				XP_090885.1	record was removed	280	4E-75
NM_008361	Mm.22150	U3.05 (5to7)		NP_000567.1	interleukin 1, beta proprotein; preinterleukin 1 beta; interleukin 1; catabin	352	3E-97
NP_032387.1				P01584	interleukin 1, beta proprotein; preinterleukin 1 beta; interleukin 1; catabin	350	1E-96
				AAA59136.1	interleukin 1	345	6E-95
				AAC03536.1	interleukin 1 beta	240	3E-63
				182779	Chain, Interleukin-1 Beta From Joint X-Ray And Nmr Refinement	239	3E-63
				220947	Chain, Interleukin-1 Beta (IL-1Beta) (Mutant With Cys 8 Replaced By Ala (C8A)	239	3E-63
				494152	Chain, Interleukin-1 Beta (Human) Mutant With Thr 9 Replaced By Gly (T9G)	239	3E-63
				230410	Chain, Interleukin-1 Beta (IL-1Beta) (Mutant With Cys 71 Replaced By Ala (C71A)	236	3E-62
				230798	Chain, Interleukin-1 Beta (IL-1Beta) (Mutant With Cys 71 Replaced By Ser (C71S)	236	4E-62
NM_013559	Mm.34828	U2.97 (YtoO)		AAC18044	antigen NY-CO-25	1529	0
NP_038587.1				BAA13192	similar to mouse heat shock protein 105 kDa beta	1524	0
				NP_006635	heat shock 105KD; heat shock 103KD alpha; heat shock 103KD beta	1465	0
				XP_114482	similar to HEAT SHOCK 70KDA PROTEIN 4 (HEAT SHOCK 70-RELATED PROTEIN APG-2) (HSP70RY)	1025	0
				BAA75062	agg-2	1021	0
				BAA75063	agg-1	951	0
				AAH00560	heat shock protein (hsp110 family)	948	0
				156208	heat shock protein 70	902	0
				CAA47886	HS24/P52	674	0
				CAA47885	HS24/P52	395	1E-108
AF127033	Mm.3760	U2.97 (YtoO)		NP_004095	fatty acid synthase	3961	0
AAG0285.1							

5

10

15

20

25

279

				GO1880	fatty-acid synthase (EC 2.3.1.85) (version 2)	3945	0
				A37788	enoyl-[acyl-carrier-protein] reductase (NADPH2, B-specific) (EC 1.3.1.10) (version 1)	3778	0
				AAH07267	Unknown (protein for IMAGE:3138929)	1533	0
				AAB3516	fatty acid synthase; FAS	728	0
				AAH07305	Unknown (protein for MGC:15706)	685	0
				AAH14634	Unknown (protein for IMAGE:353581)	553	1E-155
				NP_001366.1	deoxyribonuclease II, lysosomal; DNase II, lysosomal	520	1E-147
				NP_034192.1			
				T45071	hypothetical protein R31240_2 [imported]	494	1E-139
				NP_067056.1	deoxyribonuclease II beta, isoform 1 precursor; DNase II-like acid DNase; endonuclease DLAD	227	5E-59
				AAI34449.1	endonuclease DLAD	227	5E-59
				NP_004657.1	vanin 1 precursor; Vanin 1; pantetheinase	795	0
				AAF21453.1	ThiG66	793	0
				CAB40075.1	dJ55C23.1 (vanin 1)	793	0
				NP_060869.1	vanin 3 isoform 1 precursor; VNN3 protein; pantetheinase	657	0
				CAB40076.1	dJ55C23.2 (vanin 2)-	639	0
				NP_004656.2	vanin 2, isoform 1 precursor; Vanin 2;	638	0
				CAA10569.1	VNN2 protein	635	0
				NP_511043.1	vanin 2, isoform 2; Vanin 2;	597	1E-109
				P43251	Biotinidase precursor	382	1E-105
				NP_000051.1	biotinidase precursor	382	1E-105
				CAC33872.1	dJ55C23.5.1 (vanin 3, isoform 1)	342	1E-92
				Q14156	Hypothetical protein KIAA0143	461	0
				AKO186951			

5

10

15

20

25

280

NP_598527.1				XP_035825	similar to Hypothetical protein KIAA0143	461	0
				BAA76797	KIAA0953 protein	266	1E-136
				XP_039733	similar to KIAA0953 protein	266	1E-136
NM_011674	Mm.5160	U:2.84 (7to19)		Q16880	2-hydroxyacylsphingosine 1-beta-galactosyltransferase precursor (UDP-galactose-ceramide galactosyltransferase) (Ceramide UDP-galactosyltransferase) (Cerebroside synthase)	1042	0
NP_035804.1				NP_003351.1	UDP glycosyltransferase 8 (UDP-galactose ceramide galactosyltransferase)	1039	0
				JC5423	2-hydroxyacylsphingosine 1-beta-galactosyltransferase (EC 2.4.1.45)	1031	0
				O75795	UDP-glucuronosyltransferase 2B17 precursor, microsomal (UDP-GT)(C19-steroid specific UDP-glucuronosyltransferase)	332	1E-89
				AAC50077.1	UDP-glucuronosyltransferase precursor	329	9E-89
				AF180322.1	UDP-glucuronosyltransferase 2B15	329	9E-89
				AF297093.4	UDP-glucuronosyltransferase 1A7	326	8E-88
				NP_066307.1	UDP glycosyltransferase 1 family, polypeptide A9	323	5E-87
				AAB81536.1	UDP-glucuronosyltransferase 1A7	323	5E-87
				S11309	glucuronosyltransferase (EC 2.4.1.17)	321	3E-86
				JC5656	UDP-glucuronosyltransferase (EC 2.4.1.1-) 1A10 precursor	319	7E-86
				AF462267.1	UDP-glucuronosyltransferase UGT1A8*2	319	1E-85
				AF297093.1	UDP-glucuronosyltransferase 1A8	319	1E-85
				AAB20971	Similar to UDP glycosyltransferase 1 family, polypeptide A9	318	1E-85
				AAB84259.1	UDP-glucuronosyltransferase 1A8	316	8E-85
				NP_006789.1	UDP glycosyltransferase 2 family, polypeptide A1; UDP-glucuronosyltransferase 2 family, polypeptide A1	315	1E-84
				P36509	UDP-glucuronosyltransferase 1-2 precursor, microsomal (UDP-GT)(UGT1*2)(UGT1-1B)	315	1E-84
					(02)(UGT1.2)(UGT1A2)(UGT1B)(HLUGP4).		
				P16662	UDP-glucuronosyltransferase 2B7 precursor, microsomal (UDP-GT)(3,4-catechol estrogen specific) (UDP-GT)(2)	313	4E-84
				AAB81537.1	UDP-glucuronosyltransferase 1A10	313	5E-84

5

10

15

20

25

281

			AAH30974.1	UDP-glucosyltransferase 2 family, polypeptide B7	313	7E-84
			AAB19791.2	UDP-glucuronosyltransferase	312	9E-84
			SI7512	glucuronosyltransferase (EC 2.4.1.17)	311	3E-83
			AAF78145.1	UDP-glucuronosyltransferase	310	6E-83
			AAC95002.1	UDP-glucuronosyltransferase 2B4 precursor	309	8E-83
			JN0619	glucuronosyltransferase (EC 2.4.1.17) 2B-4 precursor	309	1E-82
			JN0620	UDP-glucuronosyltransferase (EC 2.4.1.7) 2B-10 precursor	308	2E-82
			AA323272.1	UDP-glucuronosyltransferase 2B4 precursor	306	8E-82
			AF297093_3	UDP-glucuronosyltransferase 1A6	305	1E-81
			AA27891.1	UDP-glucuronosyltransferase 2B	305	2E-81
			IF0200	orphan UDP-glucuronosyltransferase (EC 2.4.-.-)	304	2E-81
			AF297093_6	UDP-glucuronosyltransferase 1A5	304	3E-81
			AAH19861	Unknown (protein for MGC:29860)	304	3E-81
			BAB15179.1	unnamed protein product	304	3E-81
			NP_057431.1	putative N-acetyltransferase Camello 2	223	4E-58
NM_023455	Mm.154782	U:2.75 (Sto19)				
NP_075944.1			NP_003951.2	N-acetyltransferase 8: kidney- and liver-specific gene product: kidney- and liver-specific gene	216	3E-56
			BAA71643.1	GLA	216	4E-56
			AAH12626.1	kidney- and liver-specific gene	214	1E-55
			144342	hypothetical protein TSC501 (imported)	214	1E-55
NM_023478	Mm.46214	U:2.74 (Sto19)	O75631	Uroplakin III precursor (UPIII)	496	1E-140
NP_075967.1			NP_008884.1	uroplakin 3	496	1E-140
			BAA25678.1	uroplakin 3	439	1E-123
			P06576	ATP synthase beta chain, mitochondrial precursor	893	0
NM_016774	Mm.103338	U:2.73 (YtoM)				
NP_058054.1						

5

10

15

20

25

282

NP_001677				ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, beta polypeptide; ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, beta	890
AAA51808				ATP synthase beta subunit	879
CXA29095				beta-subunit (AA 1-312)	597 1E-170
NP_056953.2				peroxisome proliferative activated receptor gamma, isoform 2; PPAR-gamma; peroxisome proliferator activated receptor gamma	953
BAA18949.1				PPAR gamma2	939
S42489				peroxisome proliferator activated receptor	922
CXA62152.1				peroxisome proliferator activated receptor gamma	916
NP_005028.3				peroxisome proliferative activated receptor gamma, isoform 1; PPARG-gamma; peroxisome proliferator activated receptor gamma	914
BAA24334.1				peroxisome proliferator activated-receptor gamma	904
20150106				Chain A, Crystal Structure Of The Ligand Binding Domain Of Human Ppar-Gamma In Complex With The Agonist Az 242	511 1E-144
CAB51838				ATP-dependent metalloprotease YME1L	1341
NP_647473				YME1-like 1 isoform 1; ATP-dependent metalloprotease FtsH1 homolog	1286
AAK57555				ATP-dependent metalloprotease FtsH1 homolog	1285
AAH07795				Similar to YME1-like 1 (S. cerevisiae)	1224
AAD20962				FtsH homolog	992
CAB99462				putative ATPases	991
CAC19630				ba145E8.2 (YME1 (S.cerevisiae)-like 1)	842
NP_056537.1				calcyon	356 5E-92
NP_059692				similar to RIKEN cDNA 1700001L19 [Mus musculus]	228 9E-59

5

10

15

20

25



283

XG0796		U2.61 (YtmI)	AA09348	aldolase C	443	1E-123
CAA27422.1			CAA30270	aldolase C	443	1E-123
			CAA2861.1	aldolase A (AA 1-364)	388	1E-107
			IALD	Aldolase A (E.C.4.1.2.13)	386	1E-106
			CAA30979	aldolase A	380	1E-104
			AAB59377	aldolase B	335	4E-91
			ADHUB	Fructose-bisphosphate aldolase (EC 4.1.2.13) B	335	4E-91
			AAAS1691	aldolase B	334	9E-91
			BAA00125	aldolase B	334	9E-91
			IQ05Q	Chain Q, Fructose 1,6-Bisphosphate Aldolase From Human Liver	333	1E-90
			AAH29399	Similar to aldolase B, fructose-bisphosphate	333	1E-90
			I313294A	aldolase B	328	4E-89
NM_019415	Mm 182905	U2.6 (Sto11)	P55017	Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride cotransporter) (Na-Cl symporter)	1795	0
NP_062288.1			G01202	NaCl electroneutral Thiazide-sensitive cotransporter	1792	0
			NP_000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters), member 3	1792	0
			NP_001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1023	0
			NP_000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12 (sodium/potassium/chloride transporters)	1022	0
			AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride transporters), member 2	944	0
			PC4180	thiazide-sensitive sodium-chloride cotransporter - human (fragment)	662	0
			NP_006589.1	solute carrier family 12 (potassium/chloride transporters), member 7; potassium/chloride transporter KCC4	316	1E-84

5

10

15

20

284

				AA132454.1	sodium-potassium-chloride cotransporter	296	1E-78
				BA86690.1	KIAA1176 protein	271	4E-71
				AAG3493.1	electroneutral potassium-chloride cotransporter KCC2	271	4E-71
				NP_065759.1	solute carrier family 12, (potassium-chloride transporter) member 3	271	4E-71
A K 0 0 9 3 7	Mm.196576	U:2.57 (YtoM)		AAH07220	hypothetical protein FLJ12118	857	0
BA829596.1							
				NP_078813	hypothetical protein FLJ12118	853	0
				BA893499	OKSW-CL10	664	0
				NP_001742	cysteine-RNA ligase, isoform b, cysteine transase; cysteine-RNA synthetase	233	6E-61
				NP_644802	cysteine-RNA ligase, isoform a, cysteine transase; cysteine-RNA synthetase	233	6E-61
				AAA73901	cysteine-RNA synthetase	227	4E-59
NM_023137	Mm.140210	U:2.56 (YtoO)		AAD52982	ubiquitin-like protein FAT10	211	1E-53
NP_075626.1							
				AAH12472	Similar to diubiquitin	210	2E-53
A K 0 1 5 7 5 0	Mm.39655	U:2.56 (YtoO)		IHY3A	Chain A, Crystal Structure Of Human Estrogen Sulfotransferase V269e Mutant In The Presence Of Paps	497	1E-139
BA829956.1							
				JC229	estrogen sulfotransferase (EC 2.8.2.-)	494	1E-138
				AAH17956.1	sulfotransferase, estrogen-prefering	492	1E-138
				AAB65154.1	thyroid hormone sulfotransferase	323	4E-87
				BA24547.1	STIB2	323	4E-87
				AAH10895.1	Unknown (protein for MGC:13356)	322	1E-86
				AAA67895.1	phenol sulfotransferase	315	1E-84
				P50225	Phenol-sulfating phenol sulfotransferase I (P-PST) (Thermostable phenol sulfotransferase) (TSPST) (HAST1/HAST2) (STIA3).	313	3E-84
				AAB1316.1	aryl sulfotransferase STIA2	313	5E-84
				AAC50480.1	phenol sulfotransferase	313	5E-84
				AAH00923.1	sulfotransferase family, cytosolic, 1A, phenol-prefering, member 1	312	6E-84

5

10

15

20

25

285

			AA031317.1	aryl sulfotransferase STIA3	312	6E-84
			BAB093491.1	sulfotransferase family 1A	311	1E-83
			AA090758.1	phenol sulfotransferase	310	3E-83
			CAA59147.1	phenol-sulfating phenosulfotransferase	309	6E-83
			AA018753.1	phenol-preferring phenol sulfotransferase 2	308	1E-82
			AAC51149.1	arylamine sulfotransferase	307	2E-82
			A55451	aryl sulfotransferase (EC 2.8.2.1)	307	2E-82
			AAC99987.1	aryl sulfotransferase	300	2E-80
			AA00409.1	sulfotransferase	298	9E-80
			AAF72810.1	sulfotransferase IC2	290	2E-77
			NP_006579.1	SULT1C sulfotransferase; sulfotransferase family, cytosolic, 1C, member C2	290	2E-77
			XP_065757.1	similar to sulfotransferase, phenol preferring 2; Phenol sulfotransferase 1c1 [Rattus norvegicus]	288	9E-77
			AAF72804.1	sulfotransferase IC1	270	4E-71
			AA078553.1	hydroxysteroid sulfotransferase SULT2B1a	202	7E-51
			AA078498.1	hydroxysteroid sulfotransferase SULT2B1a	202	7E-51
			AA078499.1	hydroxysteroid sulfotransferase SULT2B1b	202	7E-51
			1EFHA	Chain A, Crystal Structure Of The Human Hydroxysteroid Sulfotransferase In The Presence Of Pap	201	2E-50
			NP_003158.1	sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA)-preferring, member 1; sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferring, member 1	201	2E-50
			AA023169.2	alcohol/hydroxysteroid sulfotransferase; hST1a	201	2E-50
			1199A	Chain A, Crystal Structure Of Human Dehydroepiandrosterone Sulfotransferase In Complex With Substrate	201	2E-50
			AAA75491.1	dehydroepiandrosterone sulfotransferase	201	2E-50
AK002693	Mm.41325	U2.55 (YtoO)	NP_477513	diacylglycerol O-acyltransferase 2 like 1; iacylglycerolacyltransferase 2-like	516	1E-145
BAB22288.1						
			AA084176	diacylglycerol acyltransferase 2	311	1E-83
			CAD38961	hypothetical protein	311	1E-83

5

10

15

20

25

286

			CAD13492	6A351K23.5 (novel protein)	258	1E-57
			BAB15436	unlabeled protein product	241	1E-52
			AA145832	similar to predicted proteins AAB54240 ID22088822 and S67138 (PID:2132925)	208	1E-52
			JCS290	protein-tyrosine-phosphatase (EC 3.1.3.48)	2649	0
			NP_573439.1	receptor protein tyrosine phosphatase psi	2647	0
			NP_573439.1	protein tyrosine phosphatase, receptor type, U isoform 1 precursor; protein tyrosine phosphatase	2642	0
				U; protein tyrosine phosphatase receptor omicron		
			NP_573438.1	protein tyrosine phosphatase, receptor type, U isoform 2 precursor; protein tyrosine phosphatase	2635	0
				U; protein tyrosine phosphatase receptor omicron		
			NP_005692.2	protein tyrosine phosphatase, receptor type, U isoform 3 precursor; protein tyrosine phosphatase	2634	0
			AAC31938.1	U; protein tyrosine phosphatase receptor omicron		
				protein tyrosine phosphatase receptor omicron		
			CAA65832.1	receptor phosphatase PCP-2	2618	0
					2505	0
			CAA65016.1	FMI protein	2437	0
			NP_002833.2	protein tyrosine phosphatase, receptor type, K precursor; protein-tyrosine phosphatase, receptor	1667	0
				type, kappa; protein-tyrosine phosphatase kappa; protein-tyrosine phosphatase kappa		
				precursor		
			Q13262	Protein-tyrosine phosphatase kappa precursor (R-FTT-kappa)	1664	0
			AAC37599.1	protein tyrosine phosphatase	1662	0
			JC6312	protein-tyrosine-phosphatase (EC 3.1.3.48)	1645	0
			CAB31346.1	d1437116.1.1 (Protein-tyrosine phosphatase (isoform 1))	1488	0
			CAB31348.1	d1437116.1.3 (Protein-tyrosine phosphatase (isoform 3))	1480	0
			CAB31347.1	d1437116.1.2 (Protein-tyrosine phosphatase (isoform 2))	1480	0
			S17669	protein-tyrosine-phosphatase (EC 3.1.3.48), receptor type mu precursor	1478	0
			NP_002836.2	protein tyrosine phosphatase, receptor type, M precursor; protein tyrosine phosphatase, receptor	1478	0
				type, mu polypeptide; protein tyrosine phosphatase mu precursor		
			1717216B	receptor-like Tyr phosphatase	1475	0

5

10

15

20

287

		BAA22952.2	KIAA0283	protein tyrosine phosphatase, receptor type, T, isoform 2 precursor; receptor protein tyrosine phosphatase	1442	0
		NP_008981.2		receptor protein tyrosine phosphatase	1435	0
		AAD09421.2		d148014.2.1 (protein tyrosine phosphatase, receptor type, K(R-PTP-KAPPA, protein tyrosine phosphatase kappa, protein tyrosine phosphatase kappa precursor), variant 1)	1427	0
		CAD54117.1		d1707K17.1 (protein tyrosine phosphatase, receptor type, T(RPTRHO, KIAA0283))	706	0
		CAA19666.1		protein tyrosine phosphatase sigma	624	1E-177
		AAC50299.1		protein tyrosine phosphatase, receptor type, sigma, isoform 1 precursor; protein tyrosine phosphatase PTPsigma	437	1E-120
		NP_002841.2		protein tyrosine phosphatase, receptor type, sigma, isoform 1 precursor; protein tyrosine phosphatase PTPsigma	437	1E-120
		AAC41749.1		protein tyrosine phosphatase delta	436	1 e-120
		NP_569077.1		protein tyrosine phosphatase, receptor type, D isoform 4 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta	436	1E-120
		NP_569075.1		protein tyrosine phosphatase, receptor type, D isoform 2 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta	436	1E-120
		NP_569076.1		protein tyrosine phosphatase, receptor type, D isoform 3 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta	436	1E-120
		CAA38068.1		protein tyrosine phosphatase	436	1E-120
		NP_570924.1		protein tyrosine phosphatase, receptor type, sigma, isoform 2 precursor; protein tyrosine phosphatase PTPsigma	434	1E-120
		NP_570923.1		protein tyrosine phosphatase, receptor type, sigma, isoform 3 precursor; protein tyrosine phosphatase PTPsigma	434	1E-120
		NP_570925.1		protein tyrosine phosphatase, receptor type, sigma, isoform 4 precursor; protein tyrosine phosphatase PTPsigma	434	1E-120
		AAC50567.1		PTPsigma	432	1E-119
		AAD09360.1		PTPsigma-(brain)	432	1E-119
		NP_569707.1		protein tyrosine phosphatase, receptor type, F, isoform 2 precursor; protein tyrosine phosphatase, receptor type, F polypeptide; receptor-linked protein-tyrosine phosphatase LAR; Leukocyte antigen-related tyrosine phosphatase; LCA-homolog	431	1E-119

288

			TDHULK	leukocyte antigen-related protein precursor	431	1E-119
			ILARA	Chain A, Crystal Structure Of The Tandem Phosphatase Domains Of Rpp Lar	425	1E-117
			AA062834.1	PTFigma [AA 324- 1926]	420	1E-115
			IRPMB	Chain B, Human Receptor Protein Tyrosine Phosphatase Mu, Domain 1	416	1E-114
			O14753	Putative transcription factor Ovo-like 1 (HvOv1)	468	1E-130
			NP_004552.1	OVO-like 1 binding protein; putative transcription factor OVO-like 1; ovo (Drosophila) homolog-like 1	367	1E-100
			NP_067043.1	zinc finger protein 339; ovo-like 2 (Drosophila)	275	3E-72
			Q9BRP0	Zinc finger protein 339	271	2E-71
			CAB45151.1	hypothetical protein, similar to (AF134804) putative zinc finger transcription factor OVO1	238	3E-61
			CAA33902	B/B' protein (AA 1-231)	240	3E-62
			AAA60151	snRNP polypeptide B.	240	3E-62
			CAB57868	snRNP B' protein	240	3E-62
			P46331	Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hN1) (Translocation-associated notch protein TAN-1)	646	0
			A40043	notch protein homolog TAN-1 precursor	4628	0
			AAA60614.1	TAN1	4482	0
			NP_077719.2	notch 2 preproprotein	2628	0
			AAG37073.1	NOTCH2 protein	2627	0
			Q04721	Neurogenic locus notch homolog protein 2 precursor (Notch 2) (hN2)	2627	0
			AAC14346.1	Notch3	2065	0
			NP_000426.1	Notch homolog 3	2065	0
			AAC15789.1	Notch 3	2065	0

5

10

15

20

25

289

			NP_004548.1	Notch homolog 4 (Drosophila); Notch, drosophila, homolog of, 4; Notch (Drosophila) homolog	1023	0
			4			
			AAC3097.1	notch4	1023	0
			BAA13116.1	NOTCH4	878	0
			AAB39007.1	transmembrane protein Jagged 1	521	1E-146
			AAC51731.1	Jagged1	521	1E-146
			NP_000205.1	jagged 1 precursor; jagged 1; jagged1 (Alagille syndrome)	521	1E-146
			AAC51323.1	transmembrane protein Jagged	521	1E-146
			AS4105	fibrillin-2 precursor	520	1E-145
			NP_001990.1	fibrillin 2	510	1E-142
			BAB55419.1	unnamed protein product	507	1E-141
			NP_000129.1	fibrillin 1; Fibrillin-1	506	1E-141
			I713408A	fibrillin	506	1E-141
			A47221	fibrillin 1 precursor - human (fragment)	506	1E-141
			CAA45118.1	fibrillin	506	1E-141
			XP_034890.4	similar to fibrillin	504	1E-141
			BAB20317.1	notch4	500	1E-139
			AAA58435	cholesterol 7-alpha hydroxylase	865	0
NM_007824	Mm.57029					
NP_031850.1			NP_000771	cytochrome P450, subfamily VIIA, polypeptide 1; cholesterol 7-alpha-hydroxylase; cholesterol 7 alpha-monooxygenase	861	0
			AAC95426	oxysterol 7alpha-hydroxylase	342	9E-93
			AAD20021	oxysterol 7alpha-hydroxylase	342	9E-93
			AAD19877	sterol 12-alpha-hydroxylase CYP8B1	298	2E-79
			AAC63037	sterol 12-alpha-hydroxylase CYP8B1	279	7E-74
			AAA61350	CYP7	239	1E-67
			BAA11910	prostaacyclin synthase	246	5E-64
			BAA07343	prostaacyclin synthase	246	9E-64
			BAA28219	prostaacyclin synthase	246	9E-64

5

10

15

20

25

## 290

				AA031785	prolactin synthase		245	2E-63
				AA031784	prolactin synthase		245	2E-63
				AA031783	prolactin synthase		242	2E-62
NM_019640	Mm.200516	U2.47 (YtoO)		CAB63033	dJ353E16.1 (phosphatidylinositol transfer protein beta)		556	1E-157
NP_062614.1								
				AAH1427	Similar to phosphatidylinositol transfer protein, beta		549	1E-155
				Q00169	Phosphatidylinositol transfer protein alpha isoform (PtdInsTP) (P1-TP-alpha)		461	1E-129
				BAA06276	phosphatidylinositol transfer protein		457	1E-128
				AAK01444	NIR2		229	3E-59
				CAA67224	homologue of Drosophila retinal degeneration B gene		229	3E-59
				AAH22230	Unknown (protein for MGC21235)		229	3E-59
				BAA95981	KIAA1457 protein		222	6E-57
				NP_065906	PVK2 N-terminal domain-interacting receptor 3, KIAA1457 protein, likely ortholog of mouse retinal degeneration B2 homolog (Drosophila) (Rdgb2)		222	6E-57
NM_019992	Mm.38392	U2.47 (YtoO)		NP_036240	BCR downstream signaling 1		465	1E-130
NP_064376.1								
NM_011076	Mm.16086	U2.45 (YtoO)		AAA59576	P glycoprotein.		2029	0
NP_035206.1								
				AAA59575	P-glycoprotein		2026	0
				NP_000918	ATP-binding cassette, sub-family B (MDR/TAP), member 1; P glycoprotein 1/multiple drug resistance 1; P-glycoprotein-1/multiple drug resistance-1; multidrug resistance 1		2023	0
				DVHU3	multidrug resistance protein 3		1702	0
				NP_061337	ATP-binding cassette, subfamily B, member 4 isoform B; P glycoprotein 3/multiple drug resistance 3; P-glycoprotein-3/multiple drug resistance-3; multiple drug resistance 3		1697	0
				NP_061338	ATP-binding cassette, subfamily B, member 4 isoform C; P glycoprotein 3/multiple drug resistance 3		1615	0



291

				resistance 3; P-glycoprotein-3/multiple drug resistance-3; multiple drug resistance 3		
				bile salt export pump		1172
				ATP-binding cassette, sub-family B (MDR/TAP), member 11; ABC member 16; MDR/TAP		1171
				subfamily, progressive familial intrahepatic cholestasis 2; bile salt export pump		0
				bile salt export pump		1170
				Similar to deoxynucleotidyltransferase, terminal		771
						0
				deoxynucleotidyltransferase, terminal; Terminal deoxynucleotidyltransferase		767
				terminal transferase		765
				terminal deoxynucleotidyltransferase		369
				polynuclease (DNA directed), mu; polynuclease (DNA-directed), mu		333
						8E-90
				forkhead box P2; forkhead (Drosophila)-like 6		521
						1E-146
				transcription factor PREAC-2		508
				forkhead box P1; forkhead (Drosophila)-like 5; Forkhead, drosophila, homolog-like 5; forkhead-related activator 1		251
						1E-142
				Similar to glucan (1,4-alpha-), branching enzyme 1 (glycogen branching enzyme, Andersen disease, glycogen storage disease type IV)		1343
				1,4-alpha-glucan branching enzyme (EC 2.4.1.18)		1341
						0
				Myeloblastin precursor (Leukocyte proteinase 3) (PR-3) (AGF7)(Wegener's autoantigen) (P29) (C-ANCA antigen) (Neutrophil proteinase 4) (NF-4).		329
						3E-89
				proteinase 3		329
				proteinase 3		3E-89
				proteinase 3 (EC 3.4.21.-) precursor [validated]		326
				proteinase 3 precursor (AA 238) (1 is 2nd base in codon)		326
				Chain C, Pr3 (Myeloblastin).		2E-88
						325
						6E-88

30

35

40

45

50

292

		AAA59558	myeloblastin		324	7E-88
		CAA39598	alternative reading frame (AA 215)		294	8E-79
		ELHUL	leukocyte elastase (EC 3.4.21.37) precursor [validated]		256	2E-67
		CAA29300	medullasin N-term.		253	2E-66
		BAA00128	medullasin		251	6E-66
		IHIIBB	Chain B, Crystal Structure Of Human Neutrophil Elastase Complexed With An Inhibitor (Gw475131).		251	6E-66
		AABI9409	medullasin [human, bone marrow, Peptide, 238 aa].		251	6E-66
		IPFFE	Chain B, Human Leukocyte Elastase (Hle) (Neutrophil Elastase (Hae)) (E.C.3.4.21.37) Complex With The Third Domain Of Turkey Ovomucoid Inhibitor (Omky3).		251	6E-66
		AAD21524	proteinase 3		251	6E-66
		1D0FA	Chain A, Crystal Structure Of Human Neutrophil Elastase With Mdl 101, 146		250	1E-65
		IHNEE	Chain E, Human Neutrophil Elastase (HNE) (E.C.3.4.21.37) (Also Referred To As Human Leukocyte Elastase (HLE)) Complex With Methoxysuccinyl-Ala-Ala-Pro-Ala Chloromethyl Ketone (MS/ACK).		249	2E-65
		1FY3A	Chain A, Ig175qIbhp, A Mutant Of Human Heparin Binding Protein (Cap37).		198	8E-50
		IAE5	Human Heparin Binding Protein		198	8E-50
		AAB59533	azurocidin		198	8E-50
		1617124A	cationic antimicrobial protein CAP37		198	8E-50
		CAA41601	azurocidin		198	8E-50
NM_007760	Mm.20396	NP_000746.2	carnitine acetyltransferase precursor, isoform 1		1151	0
NP_031786.1						
		P43155	Carnitine O-acetyltransferase (Carnitine acetylase) (CAT)		1139	0
		CAA5539.1	carnitine acetyltransferase		1124	0
		NP_003994.2	carnitine acetyltransferase isoform 2		1117	0
		NP_659006.1	carnitine acetyltransferase precursor, isoform 3		514	1E-144
		P28329	Choline O-acetyltransferase (CHOACTase) (Choline acetylase) (ChAT)		470	1E-131
		AAK08951.1	choline acetyltransferase isoform 5		470	1E-131

5

10

15

20

25

293

			NP_065574.1	choline acetyltransferase isoform 2; acetyl CoA:choline O-acetyltransferase	468	1E-130
			AAK08952.1	choline acetyltransferase isoform R	468	1E-130
			NP_066266.1	choline acetyltransferase isoform 1; acetyl CoA:choline O-acetyltransferase	465	1E-129
			T01786	choline acetyltransferase - human (fragment)	409	1E-113
NM_008151	Mm.4720	U:2.39 (7m19)	NP_005279.1	G protein-coupled receptor 12	590	1E-167
NP_032177.1			NP_005272.1	G protein-coupled receptor 3; adenylate cyclase constitutive activator	354	2E-96
			NP_005275.1	G protein-coupled receptor 6	348	1E-94
			AAA64594.1	G protein-coupled receptor	303	3E-81
NM_010846	Mm.33996	U:2.39 (YtoO)	NP_002453	myxovirus resistance protein 1; interferon inducible protein p78; interferon-regulated resistance	794	0
NP_034976.1			AAA36337	GTP-binding protein		
			AAA36337	interferon-induced Mx protein	791	0
			BAC04017	unnamed protein product	735	0
			AAH14222	Similar to myxovirus (influenza) resistance 1, homolog of murine (interferon-inducible protein p78)	710	0
			B33481	interferon-induced viral resistance protein MxB	686	0
			AAA36459	p78-related protein	686	0
			AAC08451	MX2	376	1E-102
			AAC08448	MX2	311	4E-83
			JC4305	dynamitin II - human	228	5E-58
			P50570	Dynamitin 2	226	2E-57
			NP_004936	dynamitin 2; Dynamitin II	226	2E-57
			B40671	dynamitin, internal form 2, short C-terminal form	225	4E-57
			AAA02803	dynamitin	225	4E-57
			A40671	dynamitin, internal form 1, long C-terminal form	223	1E-56
			Q9UQ16	Dynamitin 3 (Dynamitin, testicular) (T-dynamitin)	219	2E-55
			BAA74843	KIAA0820 protein	219	2E-55
			CAB66647	hypothetical protein	217	8E-55

5

10

15

20

25

294

D 0 0 2 0 8	Mm.3925	U2.39(31011)	NP_002952.1	S100 calcium-binding protein A4; 18A2, 42A; S100 calcium-binding protein A4 (calcium protein, calyasculin, metastasin, murine placental homolog); malignant transformation suppression 1	159	25-38
BAA00148.1						
NM_012050	Mm.139817	U2.38 (Y160)	AAH46356	ostromodulin	667	0
NP_036180.1						
			AAH32667	keratan	245	25-63
			NP_002716	proline arginine-rich end leucine-rich repeat protein	232	1E-59
			AAH32881	Similar to fibromodulin	205	8E-53
			CAA51418	fibromodulin	208	2E-52
			NP_002014	fibromodulin precursor	202	1E-50
			AA-85268	lumican	200	7E-50
			P51884	Lumican precursor (Keratan sulfate proteoglycan lumican) (KSPG lumican)	200	7E-50
NM_019748	Mm.29698	U2.38 (Y160)	AAH18271	SUMO-1 activating enzyme subunit 1	594	1E-168
NP_062722.1						
			AAD12785	SUMO-1 activating enzyme E1 N subunit	591	1E-167
			AAF29104	HSPC140	587	1E-166
NM_009676	Mm.26787	U2.36 (5107)	BAB40305.1	aldehyde oxidase	2204	0
NP_033806.1						
			Q06278	Aldehyde oxidase	2174	0
			NP_001150.2	aldehyde oxidase 1	2171	0
			P47989	Xanthine dehydrogenase/oxidase [Includes: Xanthine dehydrogenase (XD); Xanthine oxidase (XO) (Xanthine oxidoreductase)]	1262	0
			AA-75287.1	xanthine dehydrogenase	1261	0
			NP_000370.1	xanthine dehydrogenase; xanthine oxidase; xanthine dehydrogenase	1255	0
			XP_002472.7	similar to Xanthine dehydrogenase/oxidase	915	0
			XP_172060.1	similar to ALDEHYDE OXIDASE HOMOLOG-1; data source:SPYR, source key:Q9ESHA4	838	0

5

10

15

20

25

295

evidence:ISS-putative							
NM_008273	Mm.4931	U:2.36 (5to11)	P31277	Homeobox protein Hox-D11 (Hox-4f)		379	1E-104
NP_032299.1			NP_067015.2	homeo box D11; homeo box 4f; Hox-4.6, mouse, homolog of homeobox protein Hox-D11		377	1E-103
			NP_005514.1	homeobox protein A11; homeobox protein HOXA11; homeo box 11		226	4E-58
NM_009773	Mm.29133	U:2.35 (Mio0)	AAC19118	MAD3-like protein kinase		1439	0
NP_033003.1			AAL10712	budding uninhibited by benzimidazoles 1 beta		1437	0
			AAC33435	mitotic checkpoint protein kinase		1437	0
			AAC06260	mitotic checkpoint kinase Mad31.		1437	0
			AAH18739	budding uninhibited by benzimidazoles 1 (yeast homolog), beta		1436	0
			AAC23736	protein kinase		1436	0
NM_030127	Mm.41957	U:2.32 (Yto0)	P83110	Probable serine protease HTRA3 precursor		771	0
NP_084403.1			NP_002766.	protease, serine, 11		451	1E-125
			BAC11470	unnamed protein product		383	1E-105
			AAC97211	serine protease		371	1E-101
			AAB94569	serine protease		307	6E-82
			ILCYA	Chain A, Crystal Structure Of The Mitochondrial Serine Protease Htra2.		306	1E-81
			AAF66597.	serine protease HtrA2-p7		258	3E-67
NM_011086	Mm.38370	U:2.32 (5to11)	BAC03674.1	unnamed protein product		1860	0
NP_032216.1			Q9Y217	FYVE finger-containing phosphoinositide kinase (1-phosphatidylinositol-4-phosphate 5-kinase) (PIP5K) (PtdIns(4)P-5-kinase) (p235)		1070	0
			XP_028867.1	similar to FYVE finger-containing phosphoinositide kinase (1-phosphatidylinositol-4-phosphate kinase) (PIP5K) (PtdIns(4)P-5-kinase) (p235)		1032	0

30

35

40

45

50

296

			NP_689884.1	hypothetical protein MCC04023	572 1E-161
			XP_114261.1	similar to FYVE finger-containing phosphoinositide kinase (1-phosphatidylinositol-4-phosphate kinase) (PIP2K) (PtdIns(4)P-5-kinase) (p235)	472 1E-131
V00795	U:2.3 (5to19)		AAB28159.1	anti-colorectal carcinoma heavy chain	327 3E-89
CAA24176.1					
			XP_208769.1	similar to Ig gamma-2 chain C region	234 4E-61
			AAB21082.1	Ig gamma 2 H chain BUR	234 4E-61
			AAG00910.2	recombinant IgG2 heavy chain	233 5E-61
			CAC12842.1	immunoglobulin heavy chain constant region	233 5E-61
			P01839	Ig gamma-2 chain C region	233 5E-61
			AAAT76042.1	immunoglobulin gamma 2 heavy chain constant region	233 5E-61
			AAAT76043.1	immunoglobulin gamma 2 heavy chain constant	233 5E-61
			BAC04996.1	unnamed protein product	232 1E-60
			AAG00909.1	recombinant IgG1 heavy chain	232 2E-60
			S60339	Ig heavy chain V region precursor -	232 2E-60
			AAO17821.1	anti-rabies S057 immunoglobulin heavy chain	232 2E-60
			CAA75032.1	immunoglobulin lambda heavy chain	232 2E-60
			AAH16381.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	232 2E-60
			1605217A	Ig gamma1	232 2E-60
			BAC04226.1	unnamed protein product	232 2E-60
			AAH41037.1	Similar to immunoglobulin heavy chain 4 (serum IgG1)	232 2E-60
			BAC05203.1	unnamed protein product	232 2E-60
			BAC05009.1	unnamed protein product	232 2E-60
			BAC05186.1	unnamed protein product	232 2E-60
			AAO17823.1	anti-rabies SOJA immunoglobulin heavy chain	232 2E-60
			CAC10265.1	immunoglobulin heavy chain	231 2E-60
			CAC10256.1	immunoglobulin heavy chain	231 2E-60
			CAC10259.1	immunoglobulin heavy chain	231 2E-60
			CAC10242.1	immunoglobulin heavy chain	231 3E-60

5

10

15

20

25

297

			CAC20455.1	immunoglobulin heavy chain constant region gamma 2	230	4E-60
			GH1U	Ig gamma-1 chain C region - human	229	7E-60
			CAC20454.1	immunoglobulin heavy chain constant region gamma 1	229	7E-60
			AAC82327.1	immunoglobulin gamma-1 heavy chain constant region	229	7E-60
			AAI96263.1	immunoglobulin gamma-1 heavy chain constant region	229	7E-60
5			AAS3868.2	factor VII active site mutant immunocoujugate	229	7E-60
			AAH19046.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			AAH19337.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			AA02914.1	IgG	229	7E-60
			BAC05017.1	unnamed protein product	229	7E-60
10			BAC04208.1	unnamed protein product	229	7E-60
			AAH14258.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			AAH25314.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			AAH18747.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
15			AAH37361.1	similar to immunoglobulin heavy constant gamma 3	229	7E-60
			BAC05021.1	unnamed protein product	229	7E-60
			BAC05016.1	unnamed protein product	229	7E-60
			BAC05018.1	unnamed protein product	229	7E-60
			AAH06402.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			AAH14667.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
20			AAH26038.1	Similar to immunoglobulin heavy constant gamma 3 (G3m marker)	229	7E-60
			BAC05022.1	unnamed protein product	229	7E-60
			BAC05014.1	unnamed protein product	229	7E-60
25	NM_026189	Mm.6825	BAB21797.1	KLAA1706 protein	616	0
	NP_080465.1		XP_166595.1	similar to RUKEN cDNA 2310003P05	616	0
			BAB55076.1	unnamed protein product	616	0

298

NM_008673	Mm.14125	U2.29 (MtoO)	CAC01128	arylamine N-acetyltransferase-1	460	1E-129
NP_032699.1			AA023842	arylamine N-acetyltransferase 1	461	1E-129
			AAC24712	N-acetyltransferase-1	460	1E-128
			AAB84384	mutant arylamine N-acetyltransferase	457	1E-127
			BAA14095	arylamine N-acetyltransferase	454	1E-126
			BAA01641	arylamine N-acetyltransferase	434	1E-120
			IB34585	arylamine N-acetyltransferase (EC 2.3.1.5) 2	433	1E-120
			AAG34181	N-acetyltransferase	432	1E-120
			AAA98976	arylamine N-acetyltransferase	432	1E-120
			AAA64384	arylamine N-acetyltransferase	432	1E-120
			AAH15878	N-acetyltransferase 2 (arylamine N-acetyltransferase)	432	1E-120
			AAC03773	N-acetyltransferase	431	1E-119
			AAC14117	N-acetyltransferase	431	1E-119
			AAK51710	N-acetyltransferase 2	430	1E-119
			AAK51711	N-acetyltransferase 2	429	1E-119
					603	1E-172
NM_013739	Mm.33910	U2.29 (YtoM)	NP_079148	hypothetical protein FLJ22570		
NP_038767.1					678	
NM_016922	Mm.103414	U2.29 (YtoO)	Q99999	Galactosyl ceramide sulfoltransferase (GalCer sulfoltransferase)(Cerebroside sulfoltransferase) (3'-phosphoadenylyl sulfate: galactosylceramide 3'-sulfoltransferase) (3'-phosphoadenosine-5-phosphosulfate: GalCer sulfoltransferase).		
NP_038618.1				Similar to cerebroside(3'-phosphoadenylyl sulfate: galactosylceramide 3'-sulfoltransferase)	678	
			AAH14649	glycoprotein beta-Gal 3'-sulfoltransferase	233	6E-60
			NP_071417	beta-galactose-3-O-sulfoltransferase	224	4E-57
			AAK01945	Galbeta1-3GalNAc 3'-sulfoltransferase	211	3E-53
			AAK73365	Galbeta1-3GalNAc 3'-sulfoltransferase	211	3E-53
			CAD3686	hypothetical protein	210	4E-53
			BAB13977	unnamed protein product		

5

10

15

20

25



299

				AAH12976	beta-galactose-3-O-sulfotransferase, 4	209	7E-53
				AAL55759	unknown	207	5E-52
A F 0 4 7 2 5	Mm.42100	U:2.28 (5m11)		NP_000763.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase	704	0
AAD:13720.1				P33260	Cytochrome P450 2C18 (CYP11C18) (P450-6B/29C)	704	0
				NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	683	0
				P10632	Cytochrome P450 2C8 (CYP11C8) (P450 form 1) (P450 MP-12/MP-20) (P450 IIC2) (S-mephenytoin 4-hydroxylase)	681	0
				AAH20596	Unknown (protein for MGC22146)	680	0
				NP_000762.2	cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	679	0
				AAE23864.2	cytochrome P-450	679	0
				AAA52161.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	679	0
				BAA00123.1	cytochrome P-450	679	0
				NP_000761.2	cytochrome P450, subfamily IIC, polypeptide 8 isoform 1; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase; P450 form 1	678	0
				S66382	cytochrome P450 2C8 - human	677	0
				AAE35292.1	cytochrome P450 arachidonic acid epoxidase isoform, Cyp 2C8 [human, kidney, Peptide Partial, 485 aa]	677	0
				AAA52160.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	677	0
				F38462	S-mephenytoin 4-hydroxylase (EC 1.14.14.-) cytochrome P450 2C19	676	0
				P11713	Cytochrome P450 2C10 (CYP11C10) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)	674	0
				AAA52157.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	674	0

5

10

15

20

300

				1506290A	cytochrome P450		674	0
				152418	cytochrome P450		640	0
				AAH26305.1	cerebellum D4		583	1E-165
				NP_006029.1	leptin, ubi-d4; apoptosis response zinc finger protein		335	1E-90
				NP_036206.1	ker-d4 (mouse) homolog; hypothetical protein FLJ14079		290	4E-77
				NP_004638.1	Neuro-d4 (rat) homolog; D4, zinc and double PHD fingers, family 1		277	3E-73
				AAA19438.1	neutral amino acid transporter		676	0
				NP_003029.2	solute carrier family 1, member 4; glutamate/neutral amino acid transporter; alanine/serine/cysteine/threonine transporter		676	0
				155389	neutral amino acid transporter		673	0
				BAA94861.1	hASCT1		670	0
				A47131	Net-dependent neutral amino acid transporter SAT1		630	e-179
				AAK77026.1	sodium-dependent neutral amino acid transporter type 2 truncated isoform		365	2E-99
				AAD27806.1	sodium-dependent neutral amino acid transporter		365	2E-99
				AAD09814.1	neutral amino acid transporter		365	2E-99
				AAH00062.1	solute carrier family 1 (neutral amino acid transporter), member 5		365	2E-99
				AAC50629.1	neutral amino acid transporter B		365	4E-99
				AAD09812.1	RD114/sinuin type D retrovirus receptor		361	5E-98
				AAH14403.1	Similar to solute carrier family 1, member 7		324	7E-87
				CAA83507.1	GLAST1		271	4E-71
				AAH37310.1	solute carrier family 1 (glial high affinity glutamate transporter), member 3		271	4E-71
				S38353	glutamate transporter protein - human		267	1E-69
				AAC15754.1	EAT4_HUMAN		261	6E-68
				AAH33040.1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1		246	1E-63
				P43005	Excitatory amino acid transporter 3 (Sodium-dependent glutamate/aspartate transporter 3) (Excitatory amino-acid carrier) (Neuronal and epithelial glutamate transporter).		246	1E-63

5

10

15

20

25

301

		2017269C	excitatory AA transporter:ISOTYPE-3	246	1E-63
		2024230A	neuron-specific Glu transporter III	245	3E-63
		AAC27511.3	neuronal and epithelial glutamate transporter	245	4E-63
		AAA53215.1	HEAAC1	244	7E-63
		NP_004162.1	solute carrier family 1, member 2; H.sapiens mRNA for glutamate transporter; glutamate/aspartate transporter II; excitatory amino acid transporter 2; glial high affinity glutamate	244	1E-62
		BAA28706.1	glutamate transporter	243	2E-62
		AAA18900.1	glutamate/aspartate transporter II	243	2E-62
		CAC10342.1	d68D18.1.2 (solute carrier family 1 (glial high affinity glutamate transporter) member 2)	243	2E-62
		CAC10343.1	d68D18.1.1 (solute carrier family 1 (glial high affinity glutamate transporter) member 2)	243	2E-62
		AAH12119.1	solute carrier family 1 (glutamate transporter), member 7	238	4E-61
		CAC12702.1	bAG124.1 (solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1)	237	9E-61
		AAE53971.1	retinal glutamate transporter EAAT5	234	8E-60
		AAH15745	sprouty (Drosophila) homolog 2	567	1E-160
		XP_036349	similar to sprouty homolog 1 (Drosophila)	263	4E-69
		O43609	Sprouty homolog 1 (Spry-1)	201	3E-50
		NP_005831	sprouty homolog 3; antagonist of FGF signaling	200	4E-50
		O60437	Terplakin (195 kDa cornified envelope precursor) (190 kDa paraneoplastic pemphigus antigen)	2559	0
		NP_002696	periplakin	2559	0
		AAC17738	195 kDa cornified envelope precursor	2553	0
		BAA25494	KLAA0568 protein	1952	0
		AAD00186	envoplakin	659	0
		AAA52283	bullous pemphigoid antigen	280	1E-73
		AAB05427	plectin	278	7E-73

5

10

15

20

25

302

		Q15149	Plectin 1 (P1.TN) (PCN) (Hemidesmosomal protein 1) (HDI).	275	8E-72
		NP_056463	bullous pemphigoid antigen 1 isoform 1eA precursor, dysstemin, hemidesmosomal plaque protein	259	3E-87
		NP_065121	bullous pemphigoid antigen 1 isoform 1eB precursor; bullous pemphigoid antigen 1; bullous pemphigoid antigen 1 (230/240kD); dysstemin; hemidesmosomal plaque protein	259	3E-87
		AAI62062	bullous pemphigoid antigen 1 eB	258	1E-66
		O94833	Bullous pemphigoid antigen 1, isoforms 6/9/10 (Trabeculin-beta) (Bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein).	256	3E-66
		AAI62061	bullous pemphigoid antigen 1 eA	256	3E-66
		Q03001	Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein).	249	4E-64
		NP_036500.1	olfactory receptor, family 2, subfamily C, member 1	503	1E-141
		U:2.23 (Sto19)			
		NP_008762			
		Mm.56941			
		NP_032783.1			
		BAC05729.1	seven transmembrane helix receptor	384	1E-105
		XP_060573.1	similar to olfactory receptor MOR256-12	383	1E-105
		AAH30717.1	olfactory receptor, family 2, subfamily C, member 3	378	1E-104
		BAC05875.1	seven transmembrane helix receptor	377	1E-103
		XP_060575.1	similar to seven transmembrane helix receptor	377	1E-103
		NP_149046.1	olfactory receptor, family 2, subfamily B, member 2	371	1E-102
		XP_165701.1	similar to Olfactory receptor 2B2 (Olfactory receptor 6-1) (OR6-1) (Hs6M1-10)	370	1E-101
		Q15062	Olfactory receptor 2H3 (Olfactory receptor-like protein FAT11)	369	1E-101
		O95918	Olfactory receptor 2H2 (Hs6M1-12)	367	1E-100
		AAI98753.1	olfactory receptor	366	1E-100
		AAF98754	olfactory receptor	364	1E-100
		AAI98752.1	olfactory receptor	363	1E-99
		AAI98751.1	olfactory receptor	363	1E-99
		CAC20531.1	olfactory receptor	363	2E-99
		XP_094900.1	similar to Olfactory receptor 2H1 (Hs6M1-16) (Olfactory receptor 6-2) (OR6-2) (OLF42A-9004.14/9026.2)	361	9E-99

5

10

15

20

25

303

		CAC20478.1	olfactory receptor	358	4E-98
		XP_175276.1	similar to Olfactory receptor 213 (Olfactory receptor 6-6) (OR6-6) (Hs6M1-3)	358	6E-98
		CAC20477.1	olfactory receptor	358	6E-98
		CAC21440.1	olfactory receptor	358	7E-98
		XP_175188.1	similar to olfactory receptor	357	1E-97
5		NP_009091.1	olfactory receptor, family 2, subfamily H, member 3; Olfactory receptor 2	357	1E-97
		XP_060580.4	similar to olfactory receptor MOR256-14	356	2E-97
		BAC06162.1	seven transmembrane helix receptor	355	4E-97
		BAC05847.1	seven transmembrane helix receptor	352	5E-96
		XP_060574.6	similar to olfactory receptor, family 2, subfamily C, member 3	350	2E-95
10		P58173	Olfactory receptor 2B6 (Hs6M1-32) (Olfactory receptor 6-31) (OR6-31)	350	2E-95
		XP_167140.1	similar to Olfactory receptor 2B3 (Olfactory receptor 6-4) (OR6-4) (Hs6M1-1)	348	4E-95
		NP_112165.1	olfactory receptor, family 2, subfamily W, member 1	347	1E-94
		CAC20522.1	olfactory receptor	347	2E-94
		CAC20485.1	olfactory receptor	347	2E-94
15		CAC20523.1	olfactory receptor	346	3E-94
		XP_175187.1	similar to olfactory receptor	346	3E-94
		BAC05901.1	seven transmembrane helix receptor	341	9E-93
		XP_172292.1	similar to olfactory receptor MOR256-12	341	9E-93
20		CAC20503.1	olfactory receptor	339	3E-92
		CAC20497.1	olfactory receptor	337	1E-91
		NP_112167.1	olfactory receptor, family 2, subfamily 1, member	337	1E-91
		XP_094937.1	similar to olfactory receptor 89	323	3E-87
		XP_167135.1	similar to olfactory receptor MOR256-3	319	4E-86
		XP_060578.4	similar to olfactory receptor MOR256-12	305	4E-82
25		CAA10602.1	olfactory receptor 89	304	1E-81
		BAC05909.1	seven transmembrane helix receptor	295	6E-79
		XP_167046.2	similar to 573K1.15 (nm17M1-6 (novel) 7 transmembrane receptor (rhodopsin family)) (olfactory receptor LIKE) protein))	295	8E-79

304

				NP_110503.1	olfactory receptor, family 5, subfamily V, member 1	292	5E-78
U67189	Mm.181709	U.2.23 (YeuM)		AAM12651	regulator of G protein signalling 16	323	2E-87
AA50619.1				AAC16912	A28-RGS14p	320	2E-86
				NP_002000.1	fibroblast growth factor 7 precursor; keratocyte growth factor	352	2E-96
NM_008008	Mm.57177	U.2.22 (Sto19)					
NP_032034.1							
				NP_067023	pleckstrin homology domain containing, family B (evectins) member 1; PH domain containing protein in retina 1; PH domain containing, retina 1	450	1E-125
NM_013746	Mm.26633	U.2.22 (YeuO)		AAF21786	KPL1	415	1E-114
NP_038774.1				AAF18572	PHR1 isoform 2	364	2E-99
				AAH08075	PH domain containing protein in retina 1	330	7E-89
NM_009613	Mm.89854	U.2.22 (MuoO)		BAA32352.1	MDC/ADAM11	1454	0
NP_033743.1				O75078	ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein)	1451	0
				I65967	disintegrin-like metalloproteinase (EC 3.4.24.-), splice form 2	1345	0
				BAA06670.1	metalloprotease/disintegrin-like protein	1340	0
				S38539	disintegrin-like metalloproteinase (EC 3.4.24.-), splice form 1	1011	0
				BAA06671.1	metalloprotease/disintegrin-like protein	1008	0
				AAF22476.2	MDC2	825	0
				NP_057435.2	a disintegrin and metalloproteinase domain 22 isoform 3 proprotein; MDC2 delta	825	0
				NP_068368.2	a disintegrin and metalloproteinase domain 22 isoform 2 proprotein; MDC2 delta	825	0
				AAF3288.1	metalloprotease-like, disintegrin-like, cysteine-rich protein 2 delta	825	0
				NP_068367.1	a disintegrin and metalloproteinase domain 22 isoform 5 proprotein; MDC2 delta	825	0
				NP_004185.1	a disintegrin and metalloproteinase domain 22 isoform 4 proprotein; MDC2 delta	821	0
				Q9P0K1	ADAM 22 precursor (A disintegrin and metalloproteinase domain 22)(Metalloproteinase-like,	821	0

5

10

15

20

25

305

			disintegrin-like, and cysteine-rich protein 2) (Metalloproteinase-disintegrin ADAM22-3).		
		AAD55251.1	metalloproteinase-disintegrin ADAM22-3	821	0
		NP_003803.1	a disintegrin and metalloproteinase domain 23 preproprotein	726	0
		NP_075252.2	a disintegrin and metalloproteinase domain 19 isoform 1 preproprotein, meltrin beta	359	1E-97
		NP_150377.1	a disintegrin and metalloproteinase domain 19 isoform 2 preproprotein, meltrin beta	358	3E-97
		CAC20383.1	meltrin-beta/ADAM 19 homologue	358	3E-97
		AAG50282.1	metalloproteinase-disintegrin meltrin beta	357	7E-97
		NP_067673.1	a disintegrin and metalloproteinase domain 12 isoform 2 preproprotein; A disintegrin and metalloproteinase domain 12(Meltrin-alpha, mouse, homolog of); meltrin alpha	348	4E-94
		AAC08703.2	meltrin-S	348	4E-94
		AAC08702.2	meltrin-L precursor	348	4E-94
		NP_079496.1	a disintegrin and metalloproteinase domain 33 isoform alpha preproprotein, disintegrin and	344	4E-93
		AAM80482.1	repolysin metalloproteinase familyprotein; metalloproteinase disintegrin		
		AAF22162.1	disintegrin and metalloproteinase domain 19	344	4E-93
		CAC16509.2	dJ964F7.1 (novel disintegrin and repolysin metalloproteinase family protein)	338	3E-91
		NP_694852.1	a disintegrin and metalloproteinase domain 33 isoform beta preproprotein, disintegrin and	334	6E-90
		AAC50403.1	repolysin metalloproteinase familyprotein; metalloproteinase disintegrin	326	1E-87
		AAH14566.1	metalloproteinase/disintegrin/cysteine-rich protein precursor	320	1E-85
		AAC50404.1	a disintegrin and metalloproteinase domain 15 (meturgidin)	307	6E-82
		AAC51112.1	meturgidin precursor	307	6E-82
		AAM49575.1	disintegrin/metalloproteinase domain 9 short protein precursor	307	6E-82
		NP_001100.1	a disintegrin and metalloproteinase domain 8 precursor	302	2E-80
		NP_055080.1	a disintegrin and metalloproteinase domain 28 isoform 1 preproprotein	293	2E-77
		AAD25099.1	metalloproteinase disintegrin cysteine-rich protein, transmembrane form MDC-1m	292	2E-77
		BAA03499.2	KJAA0021 protein	291	3E-77
		NP_003804.1	a disintegrin and metalloproteinase domain 21 preproprotein	288	5E-76
				270	8E-71

30

35

40

45

50

306

A F 3 6 3 9 3	Mm.141563	U:2.21 (YtoM)	BAA90065	KIAA1541 protein	814	0
AAK53703.1						
			AAH31790	protein phosphatase 2 (formerly 2A), regulatory subunit B (PR 52), beta isoform	759	0
			XP_029744	similar to phosphoprotein phosphatase (EC 3.1.3.16) 2A BR gamma regulatory chain - human	734	0
			AAH32954	Similar to protein phosphatase 2 (formerly 2A), regulatory subunit B (PR 52), gamma isoform	731	0
			AAD20987	protein phosphatase 2A BR gamma subunit	729	0
			AAG39636	protein phosphatase 2A1 B gamma subunit IMYPNO1	728	0
NM_016894	Mm.3272	U:2.2 (Sto11)	NP_005846.1	receptor (calcitonin) activity modifying protein 1 precursor, calcitonin receptor-like receptor	231	9E-60
NP_058590.1				activity modifying protein 1		
NM_013560	Mm.13849	U:2.2 (Sto7)	NP_001531.1	heat shock 27kDa protein 1; heat shock 27kD protein 1	357	5E-98
NP_038588.1						
			AAH12292.1	Similar to heat shock 27kD protein 1	351	5E-96
			AAH62175.1	heat shock protein 27	342	2E-93
			AAH14920.1	Unknown (protein for IMAGE:3906970)	333	1E-90
			XP_066514.1	similar to heat shock 27 kDa protein (HSP 27) (Stress-responsive protein 27) (SRP27) (Estrogen-regulated 24 kDa protein) (28 kDa heat shock protein)	267	7E-71
NM_009127	Mm.140785	U:2.2 (YtoM)	NP_005054	stearoyl-CoA desaturase (delta-9-desaturase)	597	1E-170
NP_033533.1						
			O00767	Acyl-CoA desaturase (Stearoyl-CoA desaturase) (Fatty acid desaturase) (Delta(9)-desaturase).	596	1E-170
			AAH05807.	Unknown (protein for MGC:10264)	592	1E-169
			CAA73998	stearoyl CoA desaturase	589	1E-168
			AAH71040	PRO0998	579	1E-165
			EA4779	stearoyl-CoA desaturase - human (fragment)	377	1E-104
XP_208174				similar to stearoyl-CoA desaturase (delta-9-desaturase)	273	3E-73
			CAD38567	hypothetical protein	216	6E-56
NM_019977	Mm.152200	U:2.18 (YtoO)	AAF5204	unknown	540	1E-152

5

10

15

20

25



307

NP_064361.1				NP_060054	aldohyde reductase (aldose reductase) like 6; similar to mouse aldohyde reductase 6 (renal); myo- inositol oxygenase; kidney-specific protein 32	535	IE-151
				AAK00766	kidney-specific protein 32	528	IE-149
NM_031119.4	Mm.20839	U2.18 (MtoO)		AAH22387.1	Unknown (protein for MGC:24086)	793	0
NP_112471.1				BAB47393.1	organic anion transporter 3	792	0
				AAD19357.1	organic anion transporter 3	675	0
				NP_695008.1	solute carrier family 22 member 6 isoform b; renal organic anion transporter 1; para- aminolipuppate transporter	474	IE-132
				AAC70004.1	putative renal organic anion transporter 1	474	IE-132
				AAD10052.1	para-aminolipuppate transporter	472	IE-132
				NP_004781.2	solute carrier family 22 member 6 isoform a; renal organic anion transporter 1; para- aminolipuppate transporter	472	IE-131
				NP_695011.1	solute carrier family 22 member 6 isoform e; renal organic anion transporter 1; para- aminolipuppate transporter	446	IE-124
				CAB94830.1	putative organic anion transport	412	IE-114
				CAB97249.1	putative organic anion transport	410	IE-113
				AAK68156.1	RST	356	9E-97
				AAK68155.1	OAT4	354	3E-96
				NP_006663.2	solute carrier family 22 member 7 isoform a; organic anion transporter 2; liver-specific transporter	315	1E-84
				BAB68364.1	organic anion transporter 4 like protein	314	3E-84
				AAG43523.1	organic anion transporter 2	313	5E-84
				AAL12496.1	organic anion transporter 2	310	4E-83
				CAC82910.1	putative integral membrane transport protein	286	9E-76
				BAB85030.1	unnamed protein product	285	2E-75
				BAB83517.1	HUST3	283	6E-75
				BAC11483.1	unnamed protein product	262	2E-68

5

10

15

20

25

308

			BAA76350.1	organic-cation transporter-like 3	256	1E-66
			NP_700357.1	urate anion exchanger 1 isoform b; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12	226	1E-57
			BAA36712.1	OCTN2	223	1E-56
			CAA66978.1	organic cation transporter	220	6E-56
			AAH12325.1	Similar to solute carrier family 22 (organic cation transporter), member 5	220	8E-56
			NP_003050.2	solute carrier family 22 member 4; organic cation transporter 4; integral membrane transport protein	218	3E-55
			CAA04751.1	extraneuronal monoamine transporter	217	5E-55
			BAA23356.1	OCTN1	216	8E-55
			NP_003048.1	solute carrier family 22 member 1 isoform a; organic cation transporter 1	216	1E-54
			CAB95971.1	oct1_cds	215	2E-54
			CAA66977.1	organic cation transporter	214	4E-54
			CAC39443.1	organic cation transporter 3	213	7E-54
			CAC08550.1	bA288H12.2 (organic cation transporter, liver)	209	1E-52
			AAK38593.1	organic cation transporter OKB1	207	4E-52
			AAH35973.1	Similar to organic cation transporter-like 3	207	5E-52
			BAB83913.1	putative bHLH transcription factor	250	1E-65
			Q9NQ33	Achaete-scute homolog 3 (bHLH transcriptional regulator Sgr-1)	248	5E-65
			NP_065697.1	ASCL3	248	5E-65
			NP_115785	PTEN induced putative kinase 1; protein kinase BREK	801	0
			U2.16 (Yto4)			
			AAH28215	PTEN induced putative kinase 1	798	0
			AAH09534	Unknown (protein for DMAPGE:3891886)	484	1E-135
			BAC11484	unknown protein product	408	1E-112
			XP_208584	similar to RE1-silencing transcription factor (REST) co-repressor, co-repressor of Rest; Rest co-	729	0

5

10

15

20

25

309

NP_473389.1			repressor			
			NP_775858	hypothetical protein LOC283248		729
			BAA92381	KIAA1343 protein		437 1E-121
			BAA91872	unnamed protein product		437 1E-121
			BAA06686	KIAA0071		399 1E-110
			NP_055971	REST corepressor; KIAA0071 protein		399 1E-110
			AAH31608	Similar to hypothetical protein MGC23186		336 7E-97
			AAH110608	Unknown (protein for JMA GE-4157757)		330 4E-89
NM_016968	Mm.39300	U:2.16 (YtoO)	AAH26989	Similar to Olig-1 bHLH protein		310 2E-83
NP_058664.1			Q8TAK6	Oligodendrocyte transcription factor 1 (Oligo1).		310 2E-83
M62766	Mm.2226	U:2.16 (YtoM)	IHWLD	Chain D, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Rosuvastatin (Formally Known As Z44522).		432 1E-119
AAA37819.1			IHWLC	Chain C, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Rosuvastatin (Formally Known As Z44522).		432 1E-119
			IHWLB	Chain B, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Rosuvastatin (Formally Known As Z44522).		432 1E-119
			IHWLA	Chain A, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Rosuvastatin (Formally Known As Z44522).		432 1E-119
			IHWKD	Chain D, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Atorvastatin.		432 1E-119
			IHWKC	Chain C, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Atorvastatin.		432 1E-119
			IHWKB	Chain B, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Atorvastatin.		432 1E-119
			IHWKA	Chain A, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Atorvastatin.		432 1E-119
			IHWJD	Chain D, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Cerivastatin		432 1E-119
			IHWJC	Chain C, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Cerivastatin		432 1E-119
			IHWJB	Chain B, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Cerivastatin		432 1E-119
			IHWJA	Chain A, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Cerivastatin		432 1E-119

5

10

15

20

25

310

	IHWID	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Fluvastatin	432	1E-119
	IHWIC	Chain C, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Fluvastatin	432	1E-119
	IHWIB	Chain B, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Fluvastatin	432	1E-119
	IHWIA	Chain A, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Fluvastatin	432	1E-119
	IHW9D	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Simvastatin	432	1E-119
	IHW9C	Chain C, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Simvastatin	432	1E-119
	IHW9B	Chain B, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Simvastatin	432	1E-119
	IHW9A	Chain A, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Simvastatin	432	1E-119
	IHW8D	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Compactin (Also Known As Mevastatin).	432	1E-119
	IHW8C	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Compactin (Also Known As Mevastatin).	432	1E-119
	IHW8B	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Compactin (Also Known As Mevastatin).	432	1E-119
	IHW8A	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Compactin (Also Known As Mevastatin).	432	1E-119
	IDQAD	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Hmg, Coa, And NADP <sup>+</sup> .	432	1E-119
	IDQAC	Chain C, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Hmg, Coa, And NADP <sup>+</sup> .	432	1E-119
	IDQAB	Chain B, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Hmg, Coa, And NADP <sup>+</sup> .	432	1E-119
	IDQAA	Chain A, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Hmg, Coa, And NADP <sup>+</sup> .	432	1E-119
	IDQ9D	Chain D, Complex Of Catalytic Portion Of Human Hmg-Coa Reductase With Hmg Coa.	432	1E-119
	IDQ9C	Chain C, Complex Of Catalytic Portion Of Human Hmg-Coa Reductase With Hmg-Coa.	432	1E-119
	IDQ9B	Chain B, Complex Of Catalytic Portion Of Human Hmg-Coa Reductase With Hmg-Coa.	432	1E-119
	IDQ9A	Chain A, Complex Of Catalytic Portion Of Human Hmg-Coa Reductase With Hmg-Coa.	432	1E-119
	IDQ8D	Chain D, Complex Of The Catalytic Portion Of Human Hmg-Coa Reductase With Hmg And Coa	432	1E-119

5

10

15

20

311

			IDQ8C	Chain C, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Hmg And Coa	432	1E-119
			IDQ8B	Chain B, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Hmg And Coa	432	1E-119
			IDQ8A	Chain A, Complex Of The Catalytic Portion Of Human Hmg-CoA Reductase With Hmg And Coa	432	1E-119
			NP_000850	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	432	1E-119
			AAG21343	3-hydroxy-3-methylglutaryl-coenzyme A reductase	432	1E-119
			RDHUE	hydroxymethylglutaryl-CoA reductase (NADPH2) (EC 1.1.1.34)	432	1E-119
			AAA52679	3-hydroxy-3-methylglutaryl coenzyme A reductase	432	1E-119
			P04035	3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase)	432	1E-119
			AAH33692	Similar to 3-hydroxy-3-methylglutaryl-Coenzyme A reductase	432	1E-119
			NP_612471	hypothetical protein BC000993	523	1E-148
			BAB71062	unnamed protein product	521	1E-148
			BAB69025	ALS2CR15	435	1E-122
			AAC50935	islet cell autoantigen p69	271	2E-72
			AAH08640	islet cell autoantigen 1 (69kD)	271	2E-72
			I55598	diabetes-associated autoantigen p69	271	2E-72
			NP_071682	islet cell autoantigen 1 isoform 1; islet cell autoantigen 1 (69kD); islet cell autoantigen p69	271	2E-72
			AAA64977	autoantigen p69	268	1E-71
			AAH05922	Similar to islet cell autoantigen 1 (69kD)	266	7E-71
			AAH00993	Unknown (protein for MGC:5250)	234	2E-61
			NP_004959	islet cell autoantigen 1 isoform 2; islet cell autoantigen 1 (69kD); islet cell autoantigen p69	231	2E-60
			CAA06304.1	phosphodiesterase 3A	1379	0
			NP_061249.1	cGMP-inhibited 3',5'-cyclic phosphodiesterase A (Cyclic GMP-inhibited phosphodiesterase A)	1379	0
			Q14432	(CCL-PDE A)		
			NP_000912.2	phosphodiesterase 3A, cGMP-inhibited	1379	0
			A44093	cGMP-inhibited cAMP phosphodiesterase (EC 3.1.4.-), myocardial form	1378	0

5

10

15

20

25

312

				CAA64774.1	cytic nucleotide phosphodiesterase	677	0
				NP_000913.1	phosphodiesterase 3B, cGMP-inhibited	677	0
				NP_640336	testis nuclear RNA-binding protein	896	0
				BAB71416	unnamed protein product	896	0
				AAH40229	Similar to testis nuclear RNA-binding protein	892	0
				BAC04125	unnamed protein product	866	0
				NP_009725.1	breast cancer 1, early onset; breast-ovarian cancer, included	1833	0
				A54652	breast/ovarian cancer susceptibility protein BRCA1	1816	0
				NP_009233.1	breast cancer 1, early onset isoform BRCA1-delta9-10; breast-ovarian cancer, included	1773	0
				AAB61673.1	breast and ovarian cancer susceptibility protein splice variant	1694	0
				NP_009232.1	breast cancer 1, early onset isoform BRCA1-delta15-17; breast-ovarian cancer, included	1445	0
				NP_009228.1	breast cancer 1, early onset isoform BRCA1-delta2-10; breast-ovarian cancer, included	1440	0
				NP_009231.1	breast cancer 1, early onset isoform BRCA1-delta14-18; breast-ovarian cancer, included	1420	0
				NP_009230.1	breast cancer 1, early onset isoform BRCA1-delta14-17; breast-ovarian cancer, included	1419	0
				NP_009234.1	breast cancer 1, early onset isoform BRCA1-delta11; breast-ovarian cancer, included	516	1E-144
				NP_009229.1	breast cancer 1, early onset isoform BRCA1-delta9-11; breast-ovarian cancer, included	514	1E-144
				NP_009236.1	breast cancer 1, early onset isoform BRCA1-delta9-10-11b; breast-ovarian cancer, included	514	1E-144
				NP_009235.1	breast cancer 1, early onset isoform BRCA1-delta11b; breast-ovarian cancer, included	506	1E-141
				NP_005387.1	pancreatic lipase-related protein 2	748	0
				NP_000927.1	pancreatic lipase	668	0
				polb1LFB	Triacylglycerol lipase, pancreatic precursor (Pancreatic lipase) (PL	652	0
				1604419A	lipase	646	0

5

10

15

20

25

313

			NP_006220.1	pancreatic lipase-related protein 1	631	1E-180
			AAH25784.1	pancreatic lipase-related protein 1	630	1E-179
			CAA22264.1	dA149D17.1 (PDR2 (PNLIPRP2, Pancreatic Lipase Related Protein 2 Precursor, EC 3.1.1.3))	217	3E-55
				LIKE protein		
NM_010361	Mm.24118	U:2.14 (5to19)	NP_000845.1	glutathione S-transferase theta 2	375	1E-104
NP_034091.1			AAG02373.1	glutathione S-transferase theta 2	375	1E-104
			AAC13317.1	glutathione S-transferase theta 2	364	1E-101
			XP_056016.1	similar to Glutathione S-transferase theta 1 (GST class-theta) (Glutathione transferase T1-1)	239	3E-63
			NP_000844.1	glutathione S-transferase theta 1	239	4E-63
			AAH07065.1	glutathione S-transferase theta 1	236	2E-62
NM_007836	Mm.1236	U:2.14 (5to19)	NP_001915.1	growth arrest and DNA-damage-inducible, alpha: DNA-damage-inducible transcript 1; DNA damage-inducible transcript-1; DNA damage-inducible transcript 1.	314	2E-84
NP_031862.1						
			NP_002465.1	smooth muscle myosin heavy chain 11, isoform SM1	3129	0
NM_013607	Mm.3153	U:2.13 (5to19)	NP_074035.1	smooth muscle myosin heavy chain 11, isoform SM2	3083	0
NP_038635.1			AAC31665.1	Myosin heavy chain (MHY11) (5'partial)	2907	0
			NP_002464.1	myosin, heavy polypeptide 9, non-muscle	2485	0
			P35580	Myosin heavy chain, nonmuscle type B (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMHC-B)	2476	0
			A61231	myosin heavy chain nonmuscle form A	2470	0
			NP_075008.1	smooth muscle myosin heavy chain 11, isoform SM3	2180	0
			XP_044702.2	similar to Myosin heavy chain, nonmuscle type B (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMHC-B)	1933	0

5

10

15

20

314

	AAA59888.1	cellular myosin heavy chain	1916	0
	BAA36971.1	smooth muscle myosin heavy chain	1411	0
	AAH18933.1	Unknown (protein for IMAGE:4111094)	1278	0
	AAA36349.1	nonmuscle myosin heavy chain (NMHC)	1258	0
	CAA49154.1	smooth muscle myosin heavy chain	1248	0
	AAA61765.1	nonmuscle myosin heavy chain-A	1218	0
	B61231	myosin heavy chain, nonmuscle, form IIB - human (fragment)	1217	0
	NP_090248.1	myosin, heavy polypeptide 7, cardiac muscle, beta	1177	0
	CAC20413.1	beta-myosin heavy chain	1176	0
	A46762	myosin alpha heavy chain, cardiac muscle	1176	0
	P13533	Myosin heavy chain, cardiac muscle alpha isoform (MyHC-alpha)	1175	0
	CAA79675.1	cardiac alpha-myosin heavy chain	1175	0
	XP_033377.7	similar to cardiac alpha-myosin heavy chain	1175	0
	P11055	Myosin heavy chain, fast skeletal muscle, embryonic (Muscle embryonic myosin heavy chain) (SMHCB)	1174	0
	NP_060004.1	myosin, heavy polypeptide 2, skeletal muscle, adult	1174	0
	NP_060003.1	myosin, heavy polypeptide 4, skeletal muscle	1173	0
	XP_008442.4	similar to Myosin heavy chain, skeletal muscle, perinatal (MyHC-perinatal)	1172	0
	I38055	myosin heavy chain, perinatal skeletal muscle	1172	0
	NP_002461.1	myosin, heavy polypeptide 3, skeletal muscle, embryonic	1171	0
	NP_002463.1	myosin, heavy polypeptide 8, skeletal muscle, perinatal	1170	0
	CAA37068.1	cardiac beta myosin heavy chain	1165	0
	NP_005954.2	myosin, heavy polypeptide 1, skeletal muscle, adult; myosin heavy chain IIX/d	1163	0
	CAC14945.1	dlj56N5.1.1 (Continues in EmAL133324 as dlj161H23.3)	1105	0
	BAA96036.1	KIAA1512 protein	897	0

5

10

15

20



315

				smooth muscle myosin heavy chain SM1		824	0
NM_008193	Mm.3624	U2.13 (Ytom)	AAB69327.1	guanylate kinase 1		340	2E-93
NP_032219.1			NP_000849				
			AAH09914	guanylate kinase 1		340	2E-93
			AAH06249	guanylate kinase 1		340	2E-93
			AAC50659	guanylate kinase		340	2E-93
			AAC37598	guanylate kinase		340	2E-93
			S68864	guanylate kinase (EC 2.7.4.8) 1		340	2E-93
			Q16774	Guanylate kinase (GMP kinase).		340	2E-93
			AAH07369	Similar to guanylate kinase 1		311	6E-85
NM_008542	Mm.27935	U2.13 (11to19)	NP_005576.2	MAD, mothers against decapentaplegic homolog 6; Mothers against decapentaplegic, drosophila, homolog of, 6; MAD (mothers against decapentaplegic, Drosophila) homolog 6		746	0
NP_032588.1			AAC00497.1	Snad6		746	0
			AAC50792.1	Snad6		418	1E-116
			NP_005895.1	MAD, mothers against decapentaplegic homolog 7; MAD (mothers against decapentaplegic, Drosophila) homolog 7; Mothers against decapentaplegic, drosophila, homolog of, 7		298	1E-79
			AAB81354.1	Snad7 protein		298	1E-79
NM_011389	Mm.26768	U2.13 (MtoO)	AAH21299	prostate epithelium-specific Ets transcription factor		591	1E-168
NP_038919.1			NP_036523	prostate epithelium-specific Ets transcription factor		591	1E-168
			AAC95296	Ets transcription factor PDEF		591	1E-168
			BAAB9543	prostate ets		591	1E-168
NM_011067	Mm.10723	U2.12 (Ytom)	NP_038515	period 3; PERIOD, DROSOPHILA, HOMOLOG OF, 3; period circadian protein 3		1116	0
NP_035197.1			CAB76084	hypothetical protein		1116	0
			BAB32925	period (Drosophila) homolog 3 HPER3		1113	0

5

10

15

20

25

316

			P56645	Period circadian protein 3 (hPER3).	1113	0
			AAH26102	Similar to period homolog 3 (Drosophila)	597	1E-170
			NP_002607	period 1; period (Drosophila) homolog 1; hPER; Period, drosophila, homolog of; circadian pacemaker protein RIGUI	563	1E-159
			AAF15544	PER1	563	1E-159
			AAC51765	Rigi	563	1E-159
			O15534	Period circadian protein 1 (Circadian pacemaker protein Rigi) (hPER).	563	1E-159
			T00018	period protein homolog - human	563	1E-159
			BAC06326	KIAA0482 protein	563	1E-159
			BAA94085	period1	563	1E-159
			BAA22633	hPer	563	1E-159
			BAA20804	KIAA0347 protein	495	1E-139
			NP_073728	period 2 isoform 2; period, Drosophila, homolog of; 2; period circadian protein 2	495	1E-139
			O15055	Period circadian protein 2	495	1E-139
			AAH28207	Similar to period homolog 1 (Drosophila)	407	1E-112
			NP_003885	period 2 isoform 1; PERIOD, DROSOPHILA, HOMOLOG OF; 2; period circadian protein 2	206	6E-52
			BAA83709	Per2S	206	6E-52
			BAA316162	KIAA0641 protein	1406	0
			T00378	KIAA0641 protein	1229	0
			BAB6776.1	KIAA1883 protein	457	1E-127
			XP_055866.4	similar to KIAA1883 protein	457	1E-127
			NP_055731.1	KIAA1079 protein	414	1E-114
			Q16772	Glutathione S-transferase A3-3 (GST class-alpha)	264	1E-70
			NP_000838.2	glutathione S-transferase A3	263	3E-70
			A49565	glutathione transferase (EC 2.5.1.18) alpha-3 [similarity] - human	261	1E-69
			NP_665683.1	glutathione S-transferase A1; GST, class alpha, 1; glutathione S-alkyltransferase A1; glutathione	261	1E-69

5

10

15

20

25

317

			S-aryltransferase A1; S-(hydroxyalkyl)glutathione lyase A1; glutathione S-aryltransferase A1; GST-epsilon; glutathione S-transferase 2			261	1E-69
			glutathione S-transferase A3				
			glutathione transferase (EC 2.5.1.18) A2 - human			259	3E-69
			glutathione transferase (EC 2.5.1.18) alpha-2 (clone GTI12) - human			259	4E-69
			CAB92770.1 (d15217.3 (glutathione S-transferase A2)			259	3E-69
			Chain A, Glutathione S-Transferase A1-1 (EC 2.5.1.18)			259	5E-69
			glutathione S-transferase A2; glutathione S-transferase 2; GST, class alpha, 2; liver GST2; glutathione S-alkyltransferase A2; glutathione S-aryltransferase A2; S-(hydroxyalkyl)glutathione lyase A2; glutathione S-alkyltransferase A2; GST-gamma; HA subunit 2			258	6E-69
			Chain A, Glutathione Transferase A1-1 Complexed With An Ethacrynic Acid Glutathione Conjugate (Mutant R15K)			256	2E-68
			glutathione transferase (EC 2.5.1.18) - human			256	3E-68
			TPA: glutathione transferase A5				
			glutathione transferase (EC 2.5.1.18) - human			254	9E-68
			similar to Glutathione S-transferase A1 (GTI1) (HA subunit 1) (GST-epsilon) (GSTA1-1) (GST class-alpha)			253	3E-67
			XP_167100.2				
			A56801			252	5E-67
			S77958			248	7E-66
			NP_001503.1			244	1E-64
			glutathione S-transferase A4; glutathione S-alkyltransferase A4; glutathione S-aryltransferase A4; S-(hydroxyalkyl)glutathione lyase A4; glutathione S-alkyltransferase A4; glutathione transferase A4-4; GST class-alpha; glutathione S-transferase, alpha 4				
			inhibitor of DNA binding 3; dominant negative helix-loop-helix protein; Inhibitor of DNA binding 3; dominant negative, helix-loop-helix			196	3E-49
			similar to d15005.2 (Inhibitor of DNA binding 3 (dominant negative helix-loop-helix protein, IR21, HEIR-1))			195	7E-49

30

35

40

45

318

				Q02535	DNA-binding protein inhibitor ID-3 (ID-like protein inhibitor HLH IR21) (Helix-loop-helix protein HEIR-1)	193	3E-48
NM_019393	Mm.116711	U2.1 (Y6M)	CAD44530		polymyositis/scleroderma autoantigen 1	665	0
NP_062266.1					polymyositis/scleroderma autoantigen 1	655	0
				Q06265	Polymyositis/scleroderma autoantigen 1 (Autoantigen PM/Scl 1) (Polymyositis/scleroderma autoantigen 75 kDa) (P/M/Scl-75) (P75 polymyositis-scleroderma overlap syndrome associated autoantigen)	623	1E-178
				NP_005024	polymyositis/scleroderma autoantigen 1, 75kDa; polymyositis/scleroderma autoantigen 1 (75kD)	498	1E-140
				AA358384	autoantigen	498	1E-140
				G01425	nucleolar 75K autoantigen PM-Scl - human	487	1E-137
				AAA18832	PM-Scl-75 autoantigen	487	1E-137
NM_019670	Mm.28068	U2.09 (MtoO)	BAC03793		unnamed protein product	859	0
NP_062644.1				Q9NSV4	Diaphanous protein homolog 3 (Diaphanous-related formin 3) (DRE3).	734	0
				CAC17664	bA218B22.1.1 (novel protein (presumed ortholog of mouse diaphanous-related formin (DIA2)) (isoform 1))	565	0
				NP_009293	diaphanous 2 isoform 12C	550	1E-156
				CAA75869	DIA-12C protein	550	1E-156
				NP_006720	diaphanous 2 isoform 156	550	1E-156
				CAA75870	DIA-156 protein	550	1E-156
				O60879	Diaphanous protein homolog 2 (Diaphanous-related formin 2) (DRE2).	550	1E-156
				NP_112194	diaphanous homolog 3; diaphanous (Drosophila, homolog) 3	526	1E-148
				CAB70890	hypothetical protein	526	1E-148
				T46476	hypothetical protein DKFZp434C0931.1	526	1E-148
				NP_005210	diaphanous 1; Diaphanous, Drosophila, homolog of; 1; deafness, autosomal dominant 1; diaphanous (Drosophila, homolog) 1; bDial	480	1E-134
				AAC05573	diaphanous 1	480	1E-134

5

10

15

20

319

			O60610	Diaphanous protein homolog 1 (Diaphanous-related formin 1) (DRP1).	480	1E-134
			AAH07411	Unknown (protein for MGC2554)	368	1E-101
			CAC17665	bA218B22.1.2 (novel protein (presumed ortholog of mouse diaphenous-related formin (DIA2))	332	4E-90
			CAB39108	(translation of cDNA DK1Zp34C0931 (Ehr:AL137718)) (isoform 2))		
				dJ267M20.1 (diaphanous (Drosophila, homolog 2)	293	2E-78
			BAB14533	unnamed protein product	259	3E-68
			AAH24781	Similar to dishevelled associated activator of morphogenesis 2	206	2E-52
			NP_003262	transmembrane 4 superfamily member 7; tetraspan TM4SF; novel antigen 2; tetraspanin 4	444	1E-124
			AAH19314	transmembrane 4 superfamily member 7	444	1E-124
			AAH00389	transmembrane 4 superfamily member 7	444	1E-124
			AAC69717	tetraspan TM4SF; Tspan-4	444	1E-124
			AAC51864	tetraspan	444	1E-124
			A59265	tetraspan TSPAN-4 - human.	444	1E-124
			O14817	Transmembrane 4 superfamily, member 7 (Novel antigen 2) (NAG-2) (Tetraspanin-4) (Tspan-4).	444	1E-124
			NP_006666	tetraspan NET-5	271	2E-72
			AAC33839	tetraspan NET-5	271	2E-72
			O75954	Tetraspan NET-5	271	2E-72
			NP_653164	ribose 5-phosphate isomerase A (ribose 5-phosphate epimerase); RIBOSE 5-PHOSPHATE ISOMERASE	450	1E-126
			AAH15529	Similar to ribose 5-phosphate isomerase A	450	1E-126
			P49247	Ribose 5-phosphate isomerase (Phosphoriboisomerase).	450	1E-126
			NP_000793	folate receptor 1 (adult)	259	7E-69
			NP_022888	Mm.195505 U:2.08 (5w19)		
			NP_075026.1	folate-binding protein.	256	4E-68
			NP_000795	folate receptor 3 precursor	253	3E-67

5

10

15

20

25

320

				CAA49267	folate receptor	253	4E-67
				NP_000794	folate receptor 2 precursor	253	5E-67
				AAA17370	folate binding protein	248	1E-65
5	S70056	Mm.3534	U:2.08 (YtoM)	NP_001880	crystallin, zeta; quinone oxidoreductase; NADPH:quinone reductase	519	1E-147
	AAE30620.2						
	NM_011066	Mm.8471	U:2.08 (YtoC)	BAA20804	KIAA0347 protein	1800	0
	NP_035196.1						
10				NP_073728	period 2 isoform 2; period, Drosophila, homolog of; 2; period circadian protein 2	1791	0
				O15055	Period circadian protein 2	1791	0
				NP_002607	period 1; period (Drosophila) homolog 1; hPER; Period, drosophila, homolog of; circadian	827	0
					pacemaker protein RIGUI		
				AAF15544	PER1	827	0
				AACS1765	Rigui	827	0
15				O15534	Period circadian protein 1 (Circadian pacemaker protein Rigui) (hPER).	827	0
				T00018	period protein homolog	827	0
				BAC06326	KIAA0482 protein	827	0
				BAA94035	period1	827	0
				BAA22633	hPer	827	0
20				NP_003885	period 2 isoform 1; PERIOD, DROSOPHILA, HOMOLOG OF; 2; period circadian protein 2	595	0
				BAA83709	Per2S	595	0
				BAB32925	period (Drosophila) homolog 3 hPER3	550	1E-155
				P56645	Period circadian protein 3 (hPER3).	550	1E-155
25				NP_058515	period 3; PERIOD, DROSOPHILA, HOMOLOG OF; 3; period circadian protein 3	544	1E-153
				CAB76084	hypothetical protein	544	1E-153
				AAH28207	Similar to period homolog 1 (Drosophila) [Homo sapiens].	521	1E-147
				AAH26102	Similar to period homolog 3 (Drosophila) [Homo sapiens].	340	3E-92

321

L23890	Mm.4652	U2.08 (YtoM)	NP_059145.1	ephrin receptor EphB2 isoform 1 precursor; developmentally-regulated eph-related tyrosine kinase; elk-related tyrosine kinase; eph tyrosine kinase 3	1937	0
AAA72411.1			P29323	Ephrin type-B receptor 2 precursor (Tyrosine-protein kinase receptor EPH-3) (DR1) (Receptor protein-tyrosine kinase HEK5)(ERK).	1936	0
			NP_004433.2	ephrin receptor EphB2 isoform 2 precursor; developmentally-regulated eph-related tyrosine kinase; elk-related tyrosine kinase; eph tyrosine kinase 3	1934	0
			AAA99310.1	protein-tyrosine kinase	1933	0
			I78842	receptor protein-tyrosine kinase	1925	0
			BAA06506.1	tyrosine kinase precursor	1921	0
			NP_004432.1	ephrin receptor EphB1 precursor; eph tyrosine kinase 2; ephrin receptor EphB1	1493	0
			AAD02030.1	Eph-like receptor tyrosine kinase hEphB1	1469	0
			AAD02031.1	Eph-like receptor tyrosine kinase hEphB1b	1456	0
			NP_004434.2	ephrin receptor EphB3 precursor; human embryo kinase 2; EPH-like tyrosine kinase 2; tyrosine-protein kinase receptor HEK-2	1379	0
			AAB94627.1	Eph-like receptor tyrosine kinase hEphB1c	1375	0
			P54753	Ephrin type-B receptor 3 precursor (Tyrosine-protein kinase receptor HEK-2).	1375	0
			I78843	receptor protein-tyrosine kinase	1157	0
			NP_004429.1	EphA4; Hek3; TYRO1 protein tyrosine kinase; ephrin receptor EphA4	1156	0
			NP_004431.1	EphA7; Hek11; ephrin receptor EphA7	1150	0
			NP_004430.1	EphA5; Hek7; ephrin receptor EphA5	1147	0
			P29320	Ephrin type-A receptor 3 precursor (Tyrosine-protein kinase receptor ETX1) (HEK) (HEK4).	1111	0
			NP_005224.2	EphA3; Ephrin receptor EphA3 (human embryo kinase 1); eph-like tyrosine kinase 1 (human embryo kinase 1); ephrin receptor EphA3	1110	0
			P54760	Ephrin type-B receptor 4 precursor (Tyrosine-protein kinase receptor HTK).	1072	0
			NP_004435.2	ephrin receptor EphB4 precursor; Ephrin receptor EphB4 (hepatoma transmembrane kinase); Tyro 1; ephrin receptor EphB4; hepatoma transmembrane kinase	1070	0
			CAC10350.1	dJ74M1.1.1 (tyrosine kinase isoform 1)	1067	0
			CAC10351.1	dJ74M1.1.2 (tyrosine kinase isoform 2)	1066	0
			AAA20598.1	tyrosine kinase	1061	0

5

10

15

20

322

			NP_065387.1	ephrin receptor EphA9 precursor; ephrin type-A receptor Spresour; eph- and erk-related tyrosine kinase; tyrosylprotein kinase; tyrosine-protein kinase receptor esk; protein-tyrosine kinase; hydroxyaryl-protein kinase	1027	0
			AAL14195.1	receptor protein tyrosine kinase variant EphB4v	989	0
			AAH04264.1	Similar to EphB4	946	0
			A57174	protein-tyrosine kinase (BC 2.7.1.112) erk - human	926	0
			NP_004436.1	ephrin receptor EphB6 precursor; tyrosine-protein kinase-defective receptor; ephrin type-B receptor 6	912	0
			AAH37166.1	EphA2	893	0
			NP_004422.1	EphA2; ephrin receptor EphA2; epithelial cell receptor protein tyrosine kinase	888	0
			BAA95983.1	KIAA1459 protein	887	0
			AA094628.1	Eph-like receptor tyrosine kinase EphB1d	860	0
			P21709	Ephrin type-A receptor 1 precursor (Tyrosine-protein kinase receptor EPH	717	0
			AAD03638.1	Eph-family protein	713	0
			A34076	protein-tyrosine kinase (BC 2.7.1.112)	698	0
			BAA03537.1	large erk kinase	696	0
			NP_005223.1	EphA1; eph tyrosine kinase 1 erythropoietin-producing hepatoma amplified sequence; oncogene EPH; ephrin receptor EphA1; eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence); ephrin receptor EphA1	693	0
			AAG43577.1	ephrin receptor EphA3 secreted form	568	1E-161
			CAA81796.1	receptor tyrosine kinase eph	525	1E-148
			XP_209519.1	similar to Eph receptor A6 [Mus musculus]	467	1E-131
			XP_114973.3	similar to Eph receptor A6 [Mus musculus]	455	1E-127
			AAH38796.1	Similar to EphA8	444	1E-124
			AAH08655.1	Unknown (protein for IMAGE:3852708)	324	4E-88
			AAH27940.1	Unknown (protein for MGC:34493)	303	9E-82
			CAC19201	dJ189K14.1 (ephrin receptor A7)	303	9E-82
			XP_209303.1	similar to Ephrin type-A receptor 7 precursor (Tyrosine-protein kinase receptor EHK-3) (Eph homology kinase-3) (Receptor protein-tyrosine kinase HEK11)	268	3E-71

5

10

15

20



323

				NP_775912.1	hypothetical protein FLJ3655	266	1E-70
				CAA41565.2	tyrosine kinase	228	5E-59
				NP_002101.1	hemopoietic cell kinase	228	5E-59
				TVHUHC	protein-tyrosine kinase (EC 2.7.1.112) hck	228	5E-59
				BAB15482.1	unnamed protein product	228	5E-59
				CAB15606.1	dj836N17.1 (hemopoietic cell kinase)	228	5E-59
				P08631	Tyrosine-protein kinase HCK (p59-HCK/p60-HCK) (Hemopoietic cell kinase).	228	5E-59
				IQCEA	Chain A, Crystal Structure Of Hck In Complex With A Src Family- Selective Tyrosine Kinase Inhibitor	228	5E-59
				NP_005424.1	viral oncogene yes-1 homolog 1; proto-oncogene tyrosine-protein kinase YES; Yanaguchi sarcoma oncogene; cellular yes-1 protein	226	1E-58
				BAC04470.1	unnamed protein product	223	1E-57
				NP_722560.1	PTK2 protein tyrosine kinase 2 isoform a; focal adhesion kinase 1	223	2E-57
				AAH35404.1	Similar to PTK2 protein tyrosine kinase 2	223	2E-57
				NP_005598.3	PTK2 protein tyrosine kinase 2 isoform b; focal adhesion kinase 1	223	2E-57
				NP_002341.1	v-yes-1 Yanaguchi sarcoma viral related oncogene homolog; Yanaguchi sarcoma viral (v-yes-1) related oncogene homolog	222	2E-57
				AAH28733.1	Similar to PTK2 protein tyrosine kinase 2	222	2E-57
				AAB50019.1	Lyn B protein	222	2E-57
				NP_002028.1	protein-tyrosine kinase fyn isoform a, proto-oncogene tyrosine-protein kinase fyn, src/yes-related novel gene; src-like kinase; c-syn protooncogene; tyrosine kinase p59fyn(T);OKT3-induced calcium influx regulator	221	4E-57
				NP_005347.2	lymphocyte-specific protein tyrosine kinase; oncogene LCK; membrane associated protein tyrosine kinase	221	5E-57
				P06239	LCK_HUMAN Proto-oncogene tyrosine-prote	221	5E-57
				AAF34794.1	Proto-oncogene tyrosine-protein kinase LCK (P56-LCK) (LSK) (T cell-specific protein-tyrosine kinase).	221	5E-57
				CAA26485.1	c-src	220	8E-57
				NP_005408.1	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog; Protooncogene SRC; Rous	220	8E-57

5

10

15

20

324

			sarcoma; v-src avian sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog		
	1FMK		Crystal Structure Of Human Tyrosine-Protein Kinase C-Src	220	8E-57
	TVHUSC		protein-tyrosine kinase [EC 2.7.1.12] src, neuronal	220	8E-57
25	AAA36615.1		src-like tyrosine kinase (put.), putative	219	1E-56
	AAA18225.1		lymphocyte-specific protein tyrosine kinase	219	2E-56
	AAA59502.1		lymphocyte-specific protein tyrosine kinase	219	2E-56
	NP_009297.1		v-abl Abelson murine leukemia viral oncogene homolog 1 isoform b; Abelson murine leukemia	218	3E-56
	NP_005148.1		viral (v-abl) oncogene homolog 1	218	3E-56
	NP_694592.1		v-abl Abelson murine leukemia viral oncogene homolog 1 isoform a; Abelson murine leukemia	218	4E-56
30	NP_694592.1		protein-tyrosine kinase fyn isoform b; proto-oncogene tyrosine-protein kinase fyn, src/yes-related novel gene; src-like kinase; c-syn protooncogene; tyrosine kinase p59fyn(T); OKT3-induced	218	
	NP_002022.1		calcium influx regulator	218	5E-56
	AAC50116.1		fyn-related kinase	218	5E-56
	CAC27542.1		Rak	218	5E-56
	IKSWA		bA702N8.1 (fyn-related kinase)	218	5E-56
			Chain A, Structure Of Human C-Src Tyrosine Kinase (Thr338gly Mutant) In Complex With NG-Benzyl Adp	218	5E-56
35	AAB60393.1		proto-oncogene tyrosine-protein kinase	217	7E-56
	TYHUA		protein-tyrosine kinase [EC 2.7.1.12] abl	217	7E-56
	AAB60394.1		proto-oncogene tyrosine-protein kinase	217	7E-56
	P00519		Proto-oncogene tyrosine-protein kinase ABL1 (p150) (c-ABL)	217	7E-56
	IQPEA		Chain A, Structural Analysis Of The Lymphocyte-Specific Kinase Lck In Complex With Non-Selective And Src Family Selective Kinase Inhibitors	217	9E-56
	3LCK		The Kinase Domain Of Human Lymphocyte Kinase (Lck), Activated Form (Auto-Phosphorylated On Tyr394)	217	9E-56
	AAB33113.2		tyrosine kinase p59fyn(T)	216	2E-55
	IAD5A		Chain A, Src Family Kinase Hck-Amp-Ppp Complex	216	2E-55
	NP_694593.1		protein-tyrosine kinase fyn isoform c; proto-oncogene tyrosine-protein kinase fyn, src/yes-related	214	6E-55

40

325

					novel gene; src-like kinase; c-src protein oncogene; tyrosine kinase p89 <sup>fym</sup> (T) <sub>0</sub> K(T3)-induced calcium influx regulator		
				IQTDA	Chain A, Structural Analysis Of The Lymphocyte-Specific Kinase Lck In Complex With Nucleoside Phosphate Selective And Src Family Selective Kinase Inhibitors.	214	8E-55
				NP_005237.1	for (fms/fes related) tyrosine kinase (phosphoprotein NCP94), for (fms/fes related) tyrosine kinase	213	2E-54
				BAB14871.1	unnamed protein	212	3E-54
				CAC28691.1	PTK homologous protein (AA I-507)	210	8E-54
				NP_003206.1	rec protein tyrosine kinase	209	2E-53
				PIC1225	protein-tyrosine kinase [JC 2.7.1.1(12)] FAK - human	207	5E-53
				NP_005149.2	v-abl Abelson murine leukemia viral oncogene homolog 2 isoform a; Abelson-related protein; arg	207	7E-53
				NP_009298.1	v-abl Abelson murine leukemia viral oncogene homolog 2 isoform b; arg; Abelson murine leukemia viral (v-abl) oncogene homolog 2 (arg).	207	7E-53
				AAB60412.1	tyrosine kinase	206	1E-52
				NP_003319.1	LTK tyrosine kinase	206	2E-52
				BAC43747.1	truncated ZAP kinase	205	3E-52
				NP_689814.1	hypothetical protein FLJ38281	312	1E-105
				NP_69189.1	hypothetical protein FLJ90396	316	1E-101
				NP_149350.1	DKEFZP72C163 protein	304	1E-100
				BACO4610.1	unnamed protein product	304	1E-99
				NP_653290.2	hypothetical protein FLJ32191	300	5E-99
				XP_209968.1	similar to DKEFZP72C163 protein	301	8E-99
				T14757	hypothetical protein DKFZFp572C163.1	304	2E-98
				AAD23607.1	BC37295_1	309	3E-97
				BACO4309.1	unnamed protein product	317	2E-96
				NP_003427.1	zinc finger protein 135 (clone pHZ-17)	315	1E-95
				NP_066358.1	zinc finger protein 14 (KOX 6); G1OT-4 for gonadotropin inducible transcription repressor-4	319	5E-95
				BAA86512.1	KIAA1195 protein	318	5E-95

45

50

55

60

59

326

		XP_032674.1	similar to Hypothetical zinc finger protein KIAA1198	318	5E-95
		CAB94232.2	zinc finger protein	303	3E-94
		NP_003419.1	zinc finger protein 84 (HPF2)	303	3E-94
		B33891	finger protein 2 placental - human	303	3E-94
5		XP_032812.1	similar to hypothetical protein FLJ40981	301	2E-93
		NP_150630.1	KRAB zinc finger protein KR18	293	2E-93
		BAB13437.1	KIAA1611 protein	293	2E-93
		BAB15732.1	FLJ00932 protein	293	2E-93
		NP_079009.1	hypothetical protein FLJ14345	290	3E-93
10		NP_005806.1	Kruppel-type zinc finger (C2H2)	285	4E-93
		NP_085116.1	hypothetical protein FLJ21628	301	4E-93
		XP_030892.2	similar to zinc finger protein 347; zinc finger 1111	290	8E-93
		NP_689815.1	hypothetical protein FLJ40981	301	1E-92
		AAH47412.1	hypothetical protein FLJ40981	295	1E-92
15		NP_659413.1	hypothetical protein MGC26914	295	1E-92
		JE0288	Kruppel-type zinc finger protein	285	3E-92
		NP_110451.1	hypothetical protein FLJ14356	278	1E-91
		CAD39111.1	hypothetical protein	298	2E-91
		NP_008839.1	zinc finger protein 16 (KOX 9)	298	2E-91
20		P17020	Zinc finger protein 16 (Zinc finger protein KOX9)	298	2E-91
		XP_032678.2	similar to Kruppel-type zinc finger (C2H2)	275	3E-91
		AAF71790.1	ZNF180	332	1E-90
		NP_037388.1	zinc finger protein 180 (HHZ168)	332	1E-90
		BAC04532.1	unnamed protein product	294	3E-90
25		AAH07307.1	Similar to zinc finger protein 263	294	5E-90
		AAH06528.1	zinc finger protein 43 (HIT6)	280	6E-90
		NP_009084.1	zinc finger protein 208	276	8E-90
		NP_003414.1	zinc finger protein 43 (HIT6)	282	1E-89
		AAH36110.1	Similar to zinc finger protein 208	278	1E-89

327

		AAH36714.1	Unknown (protein for IMAGE4846514)	295	1E-89
		T12489	hypothetical protein DKFZp572P0920.1	295	1E-89
		XP_032810.1	similar to Zinc finger protein 20 (Zinc finger protein KOX13) (DKFZp572P0920)	295	1E-89
		BAA06541.1	KIAA0065	291	2E-89
		XP_166119.1	similar to Zinc finger protein 33A (Zinc finger protein KOX31) (JHA00946)	291	2E-89
		NP_008905.1	zinc finger protein 33a; zinc finger and ZAK associated protein with KRAB domain	291	2E-89
		CAC16114.1	bA1021019.1 (zinc finger protein 33a (KOX 31))	291	2E-89
		AAL09923.1	CTL-associated antigen KW-4 splice variant 2	283	2E-89
		NP_003421.1	zinc finger protein 91 (HPEF7, HTF10)	290	4E-89
		BAA02587.1	KIAA1349 protein	278	4E-89
		XP_047617.4	similar to Hypothetical zinc finger protein KIAA1349	278	4E-89
		Q9P278	Hypothetical zinc finger protein KIAA1349	278	4E-89
		XP_031852.2	similar to Zinc finger protein 84 (Zinc finger protein HPP2)	278	5E-89
		P51814	Zinc finger protein 41	283	1E-88
		NP_700350.1	zinc finger protein 41	283	1E-88
		CAC88162.1	bB479F17.3 (zinc finger protein 41)	283	1E-88
		A54661	zinc finger protein ZNF41 - human	283	1E-88
		NP_115973.1	zinc finger protein 347; zinc finger 1111	287	2E-88
		NP_003406.1	zinc finger protein 268	283	5E-88
		AAK09307.1	ZNF268B	283	5E-88
		AAM28195.1	zinc finger protein 325	285	9E-88
		BAB14183.1	unnamed protein product	285	9E-88
		CAD28491.1	hypothetical protein	287	1E-87
		NP_008886.1	zinc finger protein 11b (KOX 2)	291	2E-87
		NP_660016.1	zinc finger protein 23; zinc finger protein 359	281	3E-87
		P17027	Zinc finger protein 23 (Zinc finger protein KOX16) (DKFZp569D231)	281	3E-87
		CAD38678.1	hypothetical protein	281	3E-87
		AAH15765.1	Unknown (protein for MGC23189)	285	3E-87
		NP_065704.1	zinc finger protein 287	290	6E-87

5

10

15

20

25

328

		P35789	Zinc finger protein 93 (Zinc finger protein HTF34).	282	7E-87
		BA314401.1	unnamed protein product	301	8E-87
		NP_053295.1	zinc finger protein AF020591	288	2E-86
		NP_057528.1	zinc finger protein 226; Kruppel-associated box protein	277	2E-86
		AA188103.1	zinc finger protein 226	277	2E-86
		Q9NY76	Zinc finger protein 226	277	2E-86
		AA176875.1	zinc finger protein	277	2E-86
		BAC04064.1	unnamed protein product	288	4E-86
		AAH45649.1	Similar to hypothetical protein FLJ32191	270	5E-86
		BAC04764.1	unnamed protein product	272	8E-86
		NP_689475.1	hypothetical protein DKFZp71K0837	291	1E-85
		NP_006621.1	zinc finger protein 234; zinc finger protein 269	268	2E-85
		AA188104.1	ZNF234	268	2E-85
		AAH47570.1	Similar to zinc finger protein 226	277	2E-85
		AA188107.1	Hypothetical zinc finger	277	2E-85
		NP_004225.2	zinc finger protein 93 homolog; zinc finger protein homologous to mouse Zfp93; zinc finger protein homologous to Zfp93 in mouse; zinc finger protein 93 homolog (mouse)	283	4E-85
		Q14588	Zinc finger protein 234 (Zinc finger protein HZF4).	268	4E-85
		I37570	zinc finger protein	268	4E-85
		BAC05174.1	unnamed protein product	276	4E-85
		BAB47481.1	KJAA1852 protein	289	5E-85
		AA158442.1	zinc finger protein 32	289	5E-85
		AAH37209.1	Unknown (protein for MCC:41936)	289	5E-85
		XP_086070.1	similar to Zinc finger protein 93 (Zinc finger protein HTF34)	277	7E-85
		NP_060770.2	zinc finger protein 83 (HPF1)	284	7E-85
		XP_209142.1	similar to Zinc finger protein 268 (Zinc finger protein HZF3)	273	9E-85
		NP_037512.1	zinc finger protein 228	291	1E-84
		AACS1180.1	Kruppel-related zinc finger protein	297	1E-84
		CAD38551.1	hypothetical protein	273	1E-84

5

10

15

20

25

			XP_032054.2	similar to zinc finger protein 28; zinc finger factor X6	273	1E-84
			BAA92634.1	KIAA1396 protein	273	1E-84
			NP_002570	paralemmnin	550	1E-156
			O75781	Paralemmnin	548	1E-156
			BAA13400	KIAA0270	506	1E-143
			CAA76152	paralemma	451	1E-126
			CAB37401	splice variant	449	1E-126
			T00635	hypothetical protein KIAA0270	429	1E-120
			NP_443749	paralemmnin 2	215	2E-55
			AAH39306	Similar to paralemmnin 2	206	7E-53
			CAC59702	Paln2-AKAP2 fusion protein	204	3E-52
			NP_004198.1	solute carrier family 16 (monocarboxylic acid transporters), member 3; monocarboxylate transporter 3	707	0
			NP_037488.1	monocarboxylate transporter 3	424	1E-117
			O95907	Monocarboxylate transporter 3 (MCT-3)	422	1E-117
			NP_004722.1	solute carrier family 16 (monocarboxylic acid transporters), member 7; monocarboxylate transporter 2	345	1E-93
			AAH30693.1	solute carrier family 16 (monocarboxylic acid transporters), member 7	345	1E-93
			AACT0919.1	monocarboxylate transporter 2; MCT2	343	4E-93
			NP_003042.2	solute carrier family 16 (monocarboxylic acid transporters), member 1; Solute carrier family 16 (monocarboxylic acid transporters)	311	3E-83
			A55568	monocarboxylate transporter 1 - human	311	3E-83
			CAD27707.1	monocarboxylate transporter isoform 1	310	5E-83
			AAIT09942	Unknown (protein for MGC12595)	254	5E-67
			NP_060629	nudix (nucleoside diphosphate linked moiety X)-type motif 11; hypothetical protein FLJ10628	253	1E-66

330

				XP_060053	similar to nudix (nucleoside diphosphate linked moiety X)-type motif 11; hypothetical protein FLJ10628	251	3E-66
				NP_061967	nudix (nucleoside diphosphate linked moiety X)-type motif 4	236	1E-61
				AAF68858	diphosphoinositol, polyphosphate phosphohydrolase type 2 beta	233	1E-60
				AAF68855	diphosphoinositol, polyphosphate phosphohydrolase type 2 alpha	229	1E-59
				AAF68857	diphosphoinositol, polyphosphate phosphohydrolase type 2 alpha	223	7E-58
				NP_061147	acetyl-CoA synthetase isoform a; cytoplasmic acetyl-coenzyme A synthetase; acetate-CoA ligase; acyl-activating enzyme; acetate thiokinase; acetyl-CoA synthetase	1314	0
				AAH12172	Similar to acetyl-CoA synthetase	1312	0
				BAC03849	unnamed protein product	1302	0
				NP_644803	acetyl-CoA synthetase isoform b; cytoplasmic acetyl-coenzyme A synthetase; acetate-CoA ligase; acyl-activating enzyme; acetate thiokinase; acetyl-CoA synthetase	1137	0
				AAH10141	Unknown (protein for MGCC19474)	825	0
				BAB14127	unnamed protein product	824	0
				CAB61786	dJ18C9.1.1 (similar to acetyl-coenzyme A synthetase, isoform 1)	701	0
				CAB93422	dJ1161H23.1 (similar to acetyl-coenzyme A synthetase)	673	0
				AAH39261	Similar to acetyl-Coenzyme A synthetase 2	556	1E-158
				XP_042770	similar to acetyl-CoA synthetase 2 [Mus musculus]	556	1E-158
				AAH44588	similar to acetyl-Coenzyme A synthetase 2 (AMP forming)-like	548	1E-155
				CAC33037	dJ18C9.1.2 (similar to acetyl-coenzyme A synthetase, isoform 2)	525	1E-148
				CAB75500	dJ568C11.3 (novel AMP-binding enzyme similar to acetyl-coenzyme A synthetase (acetate-coA ligase))	421	1E-117
				BAC03853	unnamed protein product	404	1E-112
				BAB7475	KIAA1846 protein	335	2E-91
				NP_078836	hypothetical protein FLJ21963	325	2E-88
				CAC33039	dJ18C9.1.3 (similar to acetyl-coenzyme A synthetase, isoform 3)	218	4E-56
				NP_065117	claudin 2	357	1E-98

5

10

15

20

25



NP_057884.1								
NM_011414	Mm.1395	U:2.05 (YtoO)				NP_003055	secretory leukocyte protease inhibitor precursor; antileukoproteinas; seminal proteinase inhibitor;	1E-45
NP_035544.1							mucus proteinase inhibitor	
U899.24	Mm.24724	U:2.05 (Sto7)				NP_005389.1	protein phosphatase 1, regulatory (inhibitor) subunit 5; Phosphatase 1, regulatory/inhibitor subunit 5	1E-154
AAB49689.1						AAD33215.1	PPPIRS	545 1E-154
NM_016878	Mm.24680	U:2.04 (YtoM)				AAM10502.1	phosphatase binding 1 protein PTG	545 1E-142
NP_058574.1						NP_036232	aspartyl aminopeptidase	862 0
						AAH00653	aspartyl aminopeptidase	862 0
						BAA92014	unnamed protein product	859 0
						BAA91903	unnamed protein product	721 0
						AAH04854	Similar to aspartyl aminopeptidase	644 0
						BAB13923	unnamed protein product	456 1E-128
						AAH03040	Similar to aspartyl aminopeptidase	281 3E-75
K 0 0 4 6 3 1	Mm.18939	U:2.04 (Sto19)				Q9Z871	Phosphomannomutase 1 (PMM 1) (PMMH-22)	511 1E-144
BAB23425.1								
						NP_002667.1	phosphomannomutase 1	508 1E-143
						NP_000294.1	phosphomannomutase 2	343 4E-93
NM_023740	Mm.20387	U:2.04 (Sto11)				AAQ23766.1	PP3774	648 0
NP_076229.1								
						AAH08074.1	Similar to RIFEN cDNA I500015N03 gene	638 0
						AAH33157.1	Similar to Abl-philin 2	523 1E-148
						NP_115703.1	Abl-philin 2	452 1E-127
NM_010421	Mm.2284	U:2.04 (YtoM)				NP_000511	hexosaminidase A preproprotein; beta-hexosaminidase alpha chain; beta-N-acetylhexosaminidase;	922 0

331

5

10

15

20

25

332

NP_034551.1				N-acetyl-beta-glucosaminidase		
	AAA51827			N-acetyl-alpha-glucosaminidase prepro-polypeptide	890	0
	AAH01138			Similar to hexosaminidase A (alpha polypeptide)	764	0
	AAA51828			N-acetyl-beta-glucosaminidase prepro-polypeptide	602	1E-172
	AAA68620			beta-hexosaminidase beta-subunit	602	1E-172
	NP_000312			hexosaminidase B preproprotein; beta-hexosaminidase beta chain; beta-N-acetylhexosaminidase; N-acetyl-beta-glucosaminidase	602	1E-172
NM_010444				nuclear receptor subfamily 4, group A, member 1 isoform a; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3	936	0
NP_034574.1		U:2.04 (Mho)		orphan receptor; steroid receptor TR3		
	AAA36763			TR3 orphan receptor	933	0
	NP_006177			nuclear receptor subfamily 4, group A, member 2 isoform a; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog	506	1E-143
	NP_775265			nuclear receptor subfamily 4, group A, member 2 isoform d; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog	483	1E-136
	AA833999			NGFI-B/nur77 beta-type transcription factor homolog	478	1E-134
	NP_775263			nuclear receptor subfamily 4, group A, member 2 isoform b; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog	467	1E-131
	Q92570			Nuclear hormone receptor NOR-1 (Neuron-derived orphan receptor 1) (Mitogen induced nuclear orphan receptor)	405	1E-112
	NP_775292			nuclear receptor subfamily 4, group A, member 3 isoform b; chondrosarcoma, extraskel	405	1E-112

5

10

15

333

				myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor			
				steroid/thyroid orphan receptor homolog gene			404 IE-112
				nuclear receptor subfamily 4, group A, member 3 isoform a; chondrosarcoma, extraskeletal			404 IE-112
				myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor			
				neuron derived orphan receptor			401 IE-111
				mitogen induced nuclear orphan receptor			399 IE-111
				neuron-derived receptor NOR-1 - human			394 IE-109
				nuclear receptor subfamily 4, group A, member 1 isoform b; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3			393 IE-109
				orphan receptor; steroid receptor TR3			
				hypothetical protein			387 IE-107
				nuclear receptor subfamily 4, group A, member 2 isoform c; nur related protein-1 (mouse); human			306 9E-43
				homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type			
				transcription factor homolog			
				voltage-dependent calcium channel gamma-3 subunit; neuronal voltage-gated calcium channel gamma-3 subunit			574 IE-164
				voltage-dependent calcium channel gamma-2 subunit; stargazin; neuronal voltage-gated calcium channel gamma-2 subunit			433 IE-121
				voltage-dependent calcium channel gamma-4 subunit; neuronal voltage-gated calcium channel gamma-4 subunit			316 3E-86
				calcium channel gamma subunit 8			291 9E-79
				voltage-dependent calcium channel gamma-8 subunit; neuronal voltage-gated calcium channel gamma-8 subunit			291 9E-79
				Voltage-dependent calcium channel gamma-8 subunit (Neuronal voltage-gated calcium channel gamma-8 subunit)			291 9E-79

20

25

30

334

			AA150049	voltage-dependent calcium channel gamma-8 subunit	291	1E-78
			AAK15019	putative voltage gated calcium channel gamma-8 subunit CACNG8	227	2E-59
			NP_079092.1	Fos-related antigen	621	1E-176
			NP_003661	differentiated embryo chondrocyte expressed gene 1	658	0
			AAK49525	bHLH transcription factor DEC1	652	0
			AAH25068	basic helix-loop-helix domain containing, class B, 3	223	1E-57
			NP_110389	basic helix-loop-helix domain containing, class B, 3; bHLH protein DEC2	223	1E-57
			BAA91947.1	unnamed protein product	347	1E-109
			NP_060764.2	hypothetical protein FLJ10998	345	1E-109
			NP_699164	hypothetical protein MGC45400	150	2E-36
			NP_663633.1	glycosylated 38 kDa sperm protein C-7/8 precursor	221	4E-56
			AAH69364.1	glycosylated 38 kDa sperm protein C-7/8 precursor	216	2E-54
			NP_000758.1	cytochrome P450, subfamily IIB (phenobarbital-inducible), polypeptide 6	701	0
			AAF13602.1	cytochrome P450-2B6	692	0
			AAA32143.1	cytochrome P450-IIB	511	1E-144
			NP_002921.1	Ras-like without CAAX 2; Rac-like, expressed in neurons (Drosophila); GTP-binding protein Roc2	382	1E-105
			AAH18060.1	Rac (Drosophila)-like, expressed in neurons	380	1E-104

5

10

15

20

25

335

					AA42214.1	rti				380	1E-104
					AA42214.1	Ras family small GTP binding protein RIN				379	1E-104
					NP_008843.1	RIBA				281	6E-75
					NP_008843.1	Ras-like without CAAX 1; Ric-like, expressed in many tissues (Drosophila); GTP-binding protein				273	2E-72
					NP_000172	Roc1 glucuronidase, beta				988	0
					AA414142	Similar to glucuronidase, beta				984	0
					1BHG.A	Chain A, Human Beta-Glucuronidase At 2.6 A Resolution				962	0
					NP_005431	GTP-binding protein Rho7				420	1E-118
					AA418096	GTP-binding protein Rho7				304	6E-83
					AA447133	RhoE				284	7E-77
					NP_005159	ras homolog gene family, member E; Rho8; RhoE				284	7E-77
					1M7BA	Chain A, Crystal Structure Of Rnd3RHOE: FUNCTIONAL IMPLICATIONS				259	2E-69
					NP_055285	GTP-binding protein RHO6				235	4E-63
					NP_004419.1	ephrin A1 precursor; eph-related receptor tyrosine kinase ligand 1 (tumor necrosis factor, alpha-induced protein 4)				353	2E-97
					AA432698.1	ephrin-A1				351	8E-97
					Q13616	Cullin homolog 1 (CUL-1)				1508	0
					1ILDJA	Chain A, Structure Of The Cul1-Rbx1-Skp1-F Boxsp2 Scf Ubiquitin Ligase Complex				1478	0
					NP_003583	cullin 1				1447	0
					1LDKA	Chain A, Structure Of The Cul1-Rbx1-Skp1-F Boxsp2 Scf Ubiquitin Ligase Complex				800	0

30

35

40

45

50

336

			AAH34318	similar to cullin protein		781	0
			ILDKB	Chain B, Structure Of The Cull-1-Rbx1-Skp1-F Box&kp2 Ser Ubiquitin Ligase Complex.		687	0
			AA4449153	cullin 1		535	1E-152
			NP_003582	cullin 2		507	1E-143
			AAC51190	CUL-2		505	1E-142
			AAC50545	Hs-CUL-2		479	1E-135
			NP_003581	cullin 3		365	1E-100
			AAC36682	cullin 3		347	3E-95
			Q93034	Vasopressin-activated calcium-mobilizing receptor (VACM-1) (Cullin homolog 5) (CUL-5).		332	1E-90
			AA670253	vasopressin-activated calcium mobilizing putative receptor protein		329	9E-90
			BAA31670	KIAA0695 protein		329	1E-89
			NP_003469	Vasopressin-activated calcium-mobilizing receptor-1; Cullin-5 (vasopressin-activated calcium-mobilizing receptor-1)		329	1E-89
			Q13620	Cullin homolog 4B (CUL-4B).		328	2E-89
			NP_003579	cullin 4B; Cullin-4B		328	2E-89
			AAK16812	cullin CUL4B		325	1E-88
			AAC50546	Hs-CUL-3.		322	2E-87
			NP_003580.	cullin 4A		317	6E-86
			AA667315	Very similar and perhaps identical to Hs-CUL-4B.; 80-100% similarity to partial sequence U58091 (PID:g1381150).		315	2E-85
			BAA33146	cullin-4A		276	7E-74
			AAC50547	Hs-CUL-4A		228	2E-59
			NP_079428	hypothetical protein FLJ12660		469	1E-132
			U2.01 (Y10M4)				
			AAH24919	hypothetical protein FLJ12660		466	1E-131
			CAD62349	unnamed protein product		252	6E-67
			U2 (Y10M)				
			P22381	Tryptophanyl-tRNA synthetase (Tryptophan--tRNA ligase) (TRPRS) (TRP53) (hwRS).		860	0
			U2 (Y10M)				

5

10

15

20

25

337

NP_035840.1				CAA44450.	IFP53		858	0
				NP_004175	tryptophanyl-tRNA synthetase; interferon-induced protein 53		854	0
				CAB94199	tryptophanyl-tRNA synthetase		554	1E-157
				CAB94198	tryptophanyl-tRNA synthetase		226	6E-59

338

Subtable 1C Mixed Genes/Proteins						Score	E Value
Mouse Gene Protein	Unigene	Behavior	Human Proteins	Description			
		F:-2.07 (Y10M)					
AK004731	Mm.19	U:-2.71					
XP_148015	8058	(71o19)	CAA06265	plakophilin 2a		635	0
			NP_004563	plakophilin 2		614	1e-174
		F:-2.54 (Y1oO)					
NM_009922	Mm.43	U:-2.65					
NP_034052.1	56	(71o19)	AAH36307	Unknown (protein for IMAGE:5165518)		558	1e-159
			NP_001290	calponin 1, basic, smooth muscle, calponins, basic; Calponin 1		550	1e-156
			G02142	smooth muscle cell calponin		548	1e-156
			BAA12983	h1-calponin		510	1e-144
			NP_001830	calponin 3; calponin, acidic		396	1e-110
			NP_004359	calponin 2; Calponin 2		347	3e-95
			XP_167021	similar to calponin 2; Calponin 2		266	7e-71
			XP_070810	similar to calponin 2; h2-calponin [Mus musculus]		247	3e-65
			BAA20887	h2-calponin		228	2e-59
		F:-2.11 (Y1oM)					
NM_021291	Mm.45	U:-3.03		solute carrier family 7 cationic amino acid transporter, y+ system, member 9; solute carrier family 7, member 9; solute carrier family 7 (cationic amino acid, transporter, y+ system), member 9			
NP_067266.1	874	(51o19)	NP_055085			754	0

5

10

15

20



339

			CAB54003	glycoprotein-associated amino acid transporter hb0.+AT1	751	0
			NP_003477	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 5; Membrane protein E16; Solute carrier family 7, member 5; 4F2 light chain	347	3e-95
			AAC81479	amino acid transporter E16	347	3e-95
			BAB70708	sodium-independent neutral amino acid transporter LAT1	346	7e-95
			AAH39692	Similar to solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 5	346	7e-95
			BAA75746	4F2 light chain	346	7e-95
			CAD62619	unnamed protein product	345	2e-94
			Q9JIM01	Y4L amino acid transporter 1 (y <sup>+</sup> )-L-type amino acid transporter 1 (y <sup>+</sup> -LAT-1) (Y <sup>+</sup> -LAT1) (Monocyte amino acid permease 2) (MOP-2).	345	2e-94
			NP_055146	solute carrier family 7, (cationic amino acid transporter, y <sup>+</sup> system) member 11; cystine/glutamate transporter	344	2e-94
			NP_003973	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 7	343	5e-94
			NP_003974	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 6	337	5e-92
			Q9JHI5	Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2).	328	2e-89
			BAB40574	cystine/glutamate exchanger	328	2e-89
			NP_036376	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 8	326	4e-89
			NP_062823	solute carrier family 7, member 10; asc-type amino acid transporter 1	323	4e-88
			BAA95120	y <sup>+</sup> L amino acid transporter-1	322	1e-87
			AAF06695	L amino acid transporter-2; LAT-2	314	3e-85
			CAD62616	unnamed protein product	210	6e-54
			CAD10393	amino acid transporter	209	1e-53
			NP_620172	amino acid transporter XAT2	207	3e-53

5

10

15

20

340

		F:2.05 (Y160)							
NM_033373	Mm.20	U:~2.12							
NP_203537.1	127	(7/10/19)	BAA92054	unnamed protein product	keratin 23 isoform $\alpha$ ; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cyokeratin 23; type I intermediate filament cyokeratin; histone deacetylase inducible keratin	598	1e-171		
			NP_056330	23		597	1e-170		
			AAH28356	type I intermediate filament cyokeratin		593	1e-169		
			Q8C075	Keratin, type I cytoskeletal 23 (Cyokeratin 23) (K23) (CK 23);		591	1e-169		
			T17294	hypothetical protein DKFZp434G032.1		322	7e-88		
			NP_775320	keratin 23 isoform $\beta$ ; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cyokeratin 23; type I intermediate filament cyokeratin; histone deacetylase inducible keratin					
				23		321	2e-87		
			S37780	keratin 20, type I-like, cytoskeletal		299	6e-81		
			XP_049979	similar to Keratin, type I cytoskeletal 20 (Cyokeratin 20) (K20) (CK 20)		299	8e-81		
			P08727	Keratin, type I cytoskeletal 19 (Cyokeratin 19) (K19) (CK 19);		287	3e-77		
				keratin 19; keratin, type I cytoskeletal 19; keratin, type I, 40-kD; cyokeratin 19; 40-kDa					
			NP_002267	keratin intermediate filament precursor gene		287	3e-77		
			BAC04534	unnamed protein product		287	3e-77		
			NP_000413	keratin 17		287	3e-77		
			KRHU9	keratin 19, type I, cytoskeletal		286	7e-77		
			NP_000214	keratin 12 (Meesmann corneal dystrophy); Keratin-12; keratin 12		283	4e-76		
			NP_002266	keratin 15; keratin-15, basic; keratin-15, beta; type I cytoskeletal 15; cyokeratin 15		283	4e-76		
			P19012	Keratin, type I cytoskeletal 15 (Cyokeratin 15) (K15) (CK 15);		283	4e-76		
			NP_002265	keratin 13 isoform $\beta$ ; keratin, type I cytoskeletal 13; cyokeratin 13		281	2e-75		
			NP_705604	keratin 13 isoform $\alpha$ ; keratin, type I cytoskeletal 13; cyokeratin 13		281	2e-75		
			KRHU3	keratin 13, type I, cytoskeletal, long splice form		281	2e-75		

5

10

15

20

341

			keratin type 16	AAA59460			278	1e-74
			keratin 16; keratin, type I cytoskeletal 16; cytokeratin 16	NP_005548			278	2e-74
			keratin 16, type I, cytoskeletal	JC4313			278	2e-74
			keratin 14, type I, cytoskeletal	KRHUE			277	3e-74
			keratin 14 (epidermolysis bullosa simplex, Dowling-Meara, Koebner)	AAH02690			277	3e-74
			keratin 14; cytokeratin 14	NP_005517			277	3e-74
			type I hair keratin 6; keratin, hair, acidic, 6	NP_003762			264	3e-70
			Similar to keratin, hair, acidic, 6	AAH43581			264	3e-70
			cytokeratin 20	CAA51914			263	4e-70
			type I hair keratin 5; Ha-5; hard keratin, type I, 5	NP_002271			257	3e-68
			hypothetical protein FLJ20261	NP_061889			256	6e-68
			type I hair keratin 5	CAA76387			256	8e-68
			Keratin, type I cuticular HA5 (Hair keratin, type I HA5),	Q62764			256	8e-68
			HFHa5 hair keratin type I intermediate filament	CAA62286			256	8e-68
			similar to keratin 17	XP_039921			253	5e-67
			keratin 10 (epidermolytic hyperkeratosis; keratosis palmaris et plantaris)	AAH34697			252	9e-67
			Keratin, type I cytoskeletal 10 (Cytokeratin 10) (CK 10).	P13645			252	9e-67
			similar to keratin 17	XP_170564			252	9e-67
			type I hair keratin 3A; Ha-3; hard keratin, type I, 3; keratin, hair, acidic, 3A	NP_004129			251	2e-66
			Keratin, type I cuticular HA3-1 (Hair keratin, type I HA3-1),	OT6009			251	3e-66
			keratin 10, type I, cytoskeletal	KRHU0			250	3e-66
			type I hair keratin 1; hard keratin, type I, 1; Ha-1; keratin, hair, acidic, 1	NP_002268			249	6e-66
			Keratin, type I cuticular HA1 (Hair keratin, type I HA1).	Q15323			249	7e-66
			Keratin, type I cuticular HA4 (Hair keratin, type I HA4).	OT6011			248	1e-65
			type I hair keratin 3B; keratin, hair, acidic, 3B; Ha-3B; hard keratin, type I, 3B	NP_002270			248	2e-65
			keratin Ha1, type I, hair	S60034			247	4e-65
			hair keratin acidic 3-II	CAA57956			246	5e-65
			similar to keratin, hair, acidic, 4	AAH41070			246	6e-65

5

10

15

20

25

342

				NP_066293	type I hair keratin 4; hard keratin, type I, 4	245	1e-64
				NP_002269	type I hair keratin 2; Ha-2; hard keratin, type I, 2; keratin, hair, acidic, 2	245	1e-64
				XP_091685	similar to RIKEN cDNA 4733401L19 [Mus musculus]	244	2e-64
				Q14532	Keratin, type I cuticular HA2 (Hair keratin, type I HA2).	244	2e-64
				CAA57179	hair type I acidic keratin	244	2e-64
				NP_000215	keratin 18	243	4e-64
				CAA82315	cytokeratin 9	243	7e-64
				CAA31377	cytokeratin 18 (424 AA)	243	7e-64
				NP_000217	keratin 9; Keratin-9	243	7e-64
				I37459	keratin Ha3-II, type I, hair - human	242	9e-64
				AAH00698	keratin 18	242	1e-63
				AAA59468	keratin-10	239	6e-63
				CAA76389	type I hair keratin 7	236	5e-62
				NP_000412	keratin 10; Keratin-10	236	5e-62
				OT8015	Keratin, type I cuticular HA8 (Hair keratin, type I HA8).	236	6e-62
				NP_006762	type I hair keratin 8	236	6e-62
				AAH09754	Similar to keratin 18	233	4e-61
				NP_003761	type I hair keratin 7	232	9e-61
				BAC03847	unnamed protein product	216	9e-56
				F-2.87 (Y10)			
				U-2.78 (51019)			
X93035	Mm.43			AAH08568	Similar to chitinase 3-like 1 (cartilage glycoprotein-39)	537	1e-152
CAA63603.1	76			NP_001267	chitinase 3-like 1; cartilage glycoprotein-39	536	1e-152
				AAH38354	similar to chitinase 3-like 1 (cartilage glycoprotein-39)	535	1e-152
				NP_003456	chitinotriase; plasma methylumbelliferyl tetra-N-acetylchitotetraoside hydrolase	355	8e-98
				AAG10644	chitinotriase precursor	355	1e-97

5

10

15

20

25

343

			1LG1A	Chain A, Crystal Structure Of Human Chitinotriase In Complex With Chitobiose	345	8e-95
			NP_003991	chitinase 3-like 2; chondrocyte protein 39	340	3e-93
			Q15782	Chitinase 3-like protein 2 precursor (YKL-39) (Chondrocyte protein 39).	340	3e-93
			AAH11460	chitinase 3-like 2	340	3e-93
			AAB04534	chitinase	340	3e-93
			AAG90019	acidic mammalian chitinase precursor	319	8e-87
			AAO37816	oviductin	274	2e-73
			AAB04126	oviductal glycoprotein	273	5e-73
			NP_002548	oviductal glycoprotein 1, 120kDa (mucin 9, oviductin); mucin 9 (oviductin); oviductal glycoprotein 1, 120kD (mucin 9, oviductin)	273	5e-73
			I38605	oviductal glycoprotein	273	5e-73
			NP_068599	eosinophil chemotactic cytokine	228	9e-59
			U2.04 (MtoO)	nuclear receptor subfamily 4, group A, member 1 isoform a; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor		
NM_010444	Mm.11		F-2.6	HMR; TR3 orphan receptor; steroid receptor TR3	936	0
NP_034574.1	9	(7to11)	NP_002126		933	0
			AAA36763	TR3 orphan receptor		
				nuclear receptor subfamily 4, group A, member 2 isoform a; nur related protein-1 (mouse); human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1;		
			NP_006177	NGFI-B/nur77 beta-type transcription factor homolog	506	1e-143
				nuclear receptor subfamily 4, group A, member 2 isoform d; nur related protein-1 (mouse); human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1;		
			NP_775265	NGFI-B/nur77 beta-type transcription factor homolog	483	1e-136
			AAB33999	NGFI-B/nur77 beta-type transcription factor homolog	478	1e-134

5

1.0

1.5

344

				nuclear receptor subfamily 4, group A, member 2 isoform b; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1;	467	1e-131
			NP_775263	NGFI-B/nur77 beta-type transcription factor homolog		
			O92570	Nuclear hormone receptor NOR-1 (Neuron-derived orphan receptor 1) (Mitogen induced nuclear orphan receptor).	405	1e-112
				nuclear receptor subfamily 4, group A, member 3 isoform b; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor	405	1e-112
			NP_775292	steroid/thyroid orphan receptor homolog gene	404	1e-112
			AAB36006	nuclear receptor subfamily 4, group A, member 3 isoform a; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor	404	1e-112
			NP_008912	neuron derived orphan receptor	401	1e-111
			BAA11419	mitogen induced nuclear orphan receptor	399	1e-111
			AAB02581	nuclear receptor subfamily 4, group A, member 1 isoform b; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor	394	1e-109
			S71930	HMR3; TR3 orphan receptor; steroid receptor TR3	393	1e-109
			NP_775181	hypothetical protein	387	1e-107
			CAD38550	nuclear receptor subfamily 4, group A, member 2 isoform c; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1;	306	9e-43
			NP_775284	NGFI-B/nur77 beta-type transcription factor homolog		

345

[illegible]

5

10

15

20

346

				AAC33487	R31237_1, partial CDS	335	3e-90
				BAA96001	KIAA1477 protein	321	6e-86
				BAA07744	KIAA0096 gene product is related to a protein kinase.	285	5e-75
				P54646	5'-AMP-activated protein kinase, catalytic alpha-2 chain (AMPK alpha-2 chain)	285	6e-75
				AAF86944	HSNFRK	283	2e-74
		U1239					
		(YtoO)					
NM_010846	Mm.33	F-2.2			myxovirus resistance protein 1; interferon inducible protein p78; interferon-regulated	794	0
NP_034976.1	996	(6167)		NP_002453	resistance GTP-binding protein	791	0
				AAA36337	interferon-induced Mx protein	735	0
				BAC04017	unnamed protein product		
					Similar to myxovirus (influenza) resistance 1, homolog of murine (interferon-inducible protein		
				AAH14222	p78)	710	0
				B33481	interferon-induced viral resistance protein MxB	686	0
				AAA36459	p78-related protein	686	0
				AAC08451	MX2	376	1e-102
				AAC08448	MX2	311	4e-83
				JC4305	dynamitin II - human	228	5e-58
				P06670	Dynamitin 2	226	2e-57
				NP_004936	dynamitin 2; Dynamitin II	226	2e-57
				B40671	dynamitin, internal form 2, short C-terminal form	225	4e-57
				AAA02803	dynamitin	225	4e-57
				A40671	dynamitin, internal form 1, long C-terminal form	223	1e-56
				QBUIQ16	Dynamitin 3 (Dynamitin, testicular) (T-dynamitin)	219	2e-55
				BAA74843	KIAA0820 protein	219	2e-55
				CAB66647	hypothetical protein	217	8e-55

5

10

15

20

25



347

NM_025703	Mm.18	U:2.03 (YtoM)					
NP_079979.1	2094	F:-2.7 (5to19)	NP_699164	hypothetical protein MGC45400		150	2e-36
NM_033174	Mm.19	U:2.51 (YtoO)					
NP_149409.1	5990	F:-2.07 (5to11)	CAA33902	B/B' protein (AA 1-231)		240	3e-52
			AAA60151	snRNP polypeptide B <sub>1</sub>		240	3e-62
			CAB57888	snRNP B' protein		240	3e-52
U67189	Mm.18	U:2.23 (YtoM)					
AAB50619.1	1709	F:-3.57 (5to11)	AAM12651	regulator of G protein signalling 16		323	2e-87
			AAC16912	A28-RGS14p		320	2e-96

**Table 2****Subtable 2A: Favorable Human Protein Classes**

	Mouse Gene	Behavior	Human Protein
5	Mouse Protein NM_008341 NP_032367.1	F:13.28 (5to11)	insulin-like growth factor binding protein 1  Alternate: Similar to insulin-like growth factor binding protein 1 Alternate: small IGF-binding-protein
10	NM_009669 NP_033799.1	F:8.34 (5to7)	amylase Subclass: amylase, alpha 2A; pancreatic; Amylase, pancreatic, alpha-2A Subclass: amylase, alpha 2B; pancreatic; Amylase, pancreatic, alpha-2B
15			Subclass: amylase, alpha 1A; salivary; Amylase, salivary, alpha-1A
	NM_019824 NP_062798.1	F:5.75 (7to19)	actin related protein 2/3 complex subunit 3; ARP2/3 protein complex subunit p21 Alternate: dJ470L14.3 (novel protein similar to the Arp2/3 protein complex subunit p21-Arc (ARC21))
20			Alternate: similar to ARP2/3 complex 21 kDa subunit (P21-ARC) (Actin-related protein 2/3 complex subunit 3)
	NM_015763 NP_056578.1	F:4.93 (5to19)	Lipin Subclass: Lipin 1 Subclass: Similar to lipin 1 Subclass: lipin 2
25			
	NM_009117 NP_033143.1	F:4.72 (5to19)	serum amyloid A1 (SAA1)
30			
	NM_015805 NP_056620.1	F:4.48 (5to7)	ATPase IIA Subclass: ATPase, class 2, member b; ATPase 9B, class II; ATPase 9B, p type Subclass: dJ1114A1.1 (ATPase, class II, type 9A (KIAA0611))
35			Subclass: similar to Potential phospholipid-transporting ATPase IIA Subclass: Potential phospholipid-transporting ATPase IIB (HUSY-20)
	NM_007706 NP_031732.1	F:4.4 (YtoM)	suppressor of cytokine signaling-2; STAT induced STAT inhibitor-2; cytokine-inducible SH2 protein 2; (Cish2)
40			
	NM_008640 NP_032666.1	F:4.09 (5to19)	lysosomal-associated protein transmembrane 4 alpha; membrane nucleoside transporter; lysosomal-associated protein transmembrane 4
	AK004851 NP_598514.1	F:4.06 (5to19)	Gene 33/Mig-6; Mig-6-mitogen-inducible gene mig-6 product [human, WI-38 cells, Peptide, 462 aa]
45			

3 4 9

		Alternate: hypothetical protein DKFZp434J1114.1
	M63245 F:3.98 (Sto19)	
5	AAA91867.1	aminolevulinic acid synthase
		Subclass: aminolevulinate, delta-, synthase 1
		Subclass: 5-aminolevulinic acid synthase
		Subclass: 5-aminolevulinic acid synthase, erythroid-specific, mitochondrial precursor (Delta-aminolevulinate synthase) (Delta-ALA synthetase) (ALAS-E)
		Subclass: aminolevulinate, delta-, synthase 2; Aminolevulinate, delta-, synthase-2
10	AK005274 F:3.89 (Sto7)	hydroxyacyl glutathione hydrolase; hydroxyacyl glutathione hydrolase;
	BAB23924.1	glyoxalase 2; Hydroxyacyl glutathione hydrolase; glyoxalase II;
		hydroxyacylglutathione hydroxylase
		Alternate: similar to FHGH
	NM_026346	
15	NP_080622.1 F:3.64 (YtoO)	F-box only protein
		Subclass: F-box only protein 32 isoform 1; muscle atrophy F-box protein; atrogen-1
		Subclass: F-box only protein 32 isoform 2; muscle atrophy F-box protein; atrogen-1
		Subclass: F-box only protein 25; F-box protein Fbx25
20	NM_025298	
	NP_079574.1 F:3.45 (YtoM)	RNA polymerase III
		Subclass: RNA polymerase III 80 kDa subunit RPC5
	NM_022331 F:3.44 (Sto19)	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1; MMS-inducible gene
25	NP_071726.1	Alternate: Similar to homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1
	NM_016773 F:3.41 (YtoO)	nucleobindin
	NP_058053.1	
30		Subclass: nucleobindin 2
		Subclass: nucleobindin 1
		Subclass: Nucleobindin 1 precursor (CALNUC)
	BC017603 F:3.36 (Sto19)	unnamed protein product
35	AAH17603.1	
		Alternate: thioredoxin-related transmembrane protein
		Alternate: hypothetical protein DKFZp564E1962.1
		Alternate: hypothetical protein DJ971N18.2
40	NM_013584 F:3.35 (Sto19)	leukaemia inhibitory factor receptor, LIF receptor [human, placenta, Peptide, 1078 aa]
	NP_038612.1	Alternate: oncostatin M receptor

	NM_013590	F:3.34 (7to19)	lysozyme precursor
	NP_038618.1		
5	AK005546	F:3.33 (5to19)	
	BAB24114.1		coagulation factor
			Subclass: plasma coagulation factor XI precursor, isoform a; plasma
			thromboplastin antecedent
			Subclass: coagulation factor XI
			Subclass: platelet coagulation factor XI, isoform b; plasma thromboplastin
10			antecedent
			Alternate: plasma kallikrein B1 precursor; Kallikrein, plasma; kallikrein 3 ,
			plasma; kallikrein B plasma; Fletcher factor
	NM_010286	F:3.32 (5to19)	Glucocorticoid-induced leucine zipper protein (Delta sleep-inducing peptide
	NP_034416.1		immunoreactor) (DSIP-immunoreactive peptide) (DIP protein) (hDIP) (TSC-
			22-like protein) (TSC-22R)
15	NM_009344	F:3.29 (7to19)	T-cell death associated gene
	NP_033370.1		
			Alternate: pleckstrin homology-like domain, family A, member 1; PQ-rich
			protein
	AK005535	F:3.25 (YtoM)	solute carrier family 39 (zinc transporter), member 4
20	BAB24106.1		
	NM_009864	F:3.24 (YtoO)	Cadherin
	NP_033994.1		
			Subclass: cadherin 1, type 1 preproprotein; calcium-dependent adhesion
			protein, epithelial; cadherin 1, E-cadherin (epithelial); uvomorulin; cell-
25			CAM 120/80; Arc-1
			Subclass: cadherin 2, type 1 preproprotein; N-cadherin 1; cadherin 2, N-
			cadherin (neuronal); neural cadherin; calcium-dependent adhesion protein,
			neuronal
			Subclass: cadherin 3, type 1 preproprotein; P-cadherin; placental cadherin;
			cadherin 3, P-cadherin (placental); calcium-dependent adhesion protein,
			placental
			Subclass: cadherin 4, type 1 preproprotein; cadherin 4, R-cadherin (retinal);
			R-cadherin; retinal cadherin
			Alternate: uvomorulin
			Alternate: unnamed protein product
30			
	NM_007687	F:3.24 (5to7)	
	NP_031713.1		cofilin
			Subclass: cofilin 1 (non-muscle)
			Subclass: cofilin 2 isoform 1
35			Subclass: similar to Cofilin, non-muscle isoform (18 kDa

351

		phosphoprotein)(P18)
		Alternate: destrin (actin depolymerizing factor); destrin
40	NM_008904 NP_032930.1	F:3.2 (YtoM) peroxisome proliferative activated receptor, gamma, coactivator 1
	AK005989 BAB24354.1	F:3.2 (YtoM) protein disulfide isomerase-related protein
		Subclass: protein disulfide isomerase-related protein 5
45	NM_026508 NP_080784.1	F:3.15 (YtoM) tumor necrosis factor type 1 receptor associated protein TRAP-1
		Alternate: Unknown (protein for MGC:15157)
		Alternate: heat shock protein 75
		Alternate: tumor rejection antigen (gp96) 1; Tumor rejection antigen-1 (gp96)
50		Alternate: unnamed protein product
		Alternate: Unknown (protein for MGC:3823)
	NM_021792 NP_068564.1	F:3.14 (Sto19) hypothetical protein R30953_1
55	NM_025404 NP_079680.1	F:3.11 (Sto11) ADP-ribosylation factor
		Subclass: ADP-ribosylation factor 4-like; ADP-ribosylation factor-like 6
		Subclass: similar to ADP-ribosylation factor 4L
60		Subclass: ADP-ribosylation factor-like 7
		Subclass: ADP-ribosylation factor 4
	AK005035 BAB23762.1	F:3.09 (Sto19) transferrin
65		Alternate: Serum Transferrin
		Alternate: Lactoferrin
		Subclass: Lactoferrin (Diferic)
		Subclass: Lactoferrin (Apo Form)
		Subclass: Lactoferrin (Copper and Oxalate Form)
70		Subclass: neutrophil lactoferrin
		Subclass: Lactotransferrin precursor (Lactoferrin) [Contains: Lactoferroxin A; Lactoferroxin B; Lactoferroxin C]
	NM_009883 NP_034013.1	F:3.09 (Sto19) CCAAT/enhancer binding protein (C/EBP), beta; CCAAT/enhancer-binding protein (C/EBP), beta (transcription factor-5)
75	NM_021301 NP_067276.1	F:3.08 (YtoM) solute carrier
		Subclass: solute carrier family 15 (H+/peptide transporter), member 2
		Subclass: solute carrier family 15 (oligopeptide transporter), member 1;
		Human peptide transporter (HPEPT1) mRNA, complete cds
80		Subclass: Caco-2 oligopeptide transporter
	NM_013786	F:3.08 (YtoM) sterol/retinol dehydrogenase

5	NP 038814.1		Subclass: 3-hydroxysteroid epimerase; oxidative 3-alpha-hydroxysteroid-dehydrogenase; 3(alpha->beta)-hydroxysteroid epimerase; retinol dehydrogenase; oxidoreductase; NAD+ -dependent 3 alpha-hydroxysteroid dehydrogenase
			Subclass: <del>microsomal</del> NAD+-dependent retinol dehydrogenase 4
			Subclass: orphan short-chain dehydrogenase / reductase; retinol dehydrogenase similar protein
			Subclass: NADP-dependent retinol dehydrogenase/reductase; 3-alpha hydroxysteroid dehydrogenase
			Subclass: 11-cis retinol dehydrogenase (11-cis RDH).
10			Subclass: retinol dehydrogenase homolog isoform-1
			Subclass: retinol dehydrogenase 5 (11-cis and 9-cis); retinol dehydrogenase 5 (11-cis and 9-cis)
15	NM_016917	F:3.08 (7to19)	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 3; ferroportin 1; iron regulated gene 1; ferroportin 1
	NP 058613.1		
	NM_010004	F:3.08 (5to19)	
	NP 034134.1		cytochrome P450, subfamily II
			Subclass: cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase
20			Subclass: cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase
			Subclass: Cytochrome P450 2C9 (CYP11C9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP).
			Subclass: Cytochrome P450 2C8 (CYP11C8) (P450 form 1) (P450 MP-12/MP-20) (P450 IIC2) (S-mephenytoin 4-hydroxylase)
			Subclass: cytochrome P450 2E1
25	AB060274		
	BAB41208.1	F:3.04 (YtoM)	endothelial cell growth factor
			Subclass: endothelial cell growth factor 1 (platelet-derived); thymidine phosphorylase; gliostatin
	NM_018887	F:3 (7to19)	oxysterol 7 alpha-hydroxylase
30	NP 061375.1		
	NM_024406	F:2.98 (7to19)	fatty acid binding protein 4, adipocyte; A-FABP
	NP 077717.1		
	NM_018746	F:2.96 (YtoM)	Inter-alpha-trypsin inhibitor
	NP 061216.1		Subclass: Inter-alpha-trypsin inhibitor heavy chain H4 precursor (ITI heavy

353

		chain H4) (Inter-alpha-inhibitor heavy chain 4) (Inter-alpha-trypsin inhibitor family heavy chain-related protein) (IHRP) (Plasma kallikrein sensitive glycoprotein 120) (PK-120) (GP120) (PRO1851) [Contains: GP57]
35		Subclass: pre-alpha (globulin) inhibitor, H3 polypeptide; Inter-alpha (globulin) inhibitor, H3 polypeptide
		Subclass: Inter-alpha-trypsin inhibitor heavy chain H1 precursor (ITI heavy chain H1) (Inter-alpha-inhibitor heavy chain 1) (Inter-alpha-trypsin inhibitor complex component III) (Serum-derived hyaluronan-associated protein) (SHAP)
		Subclass: Inter-alpha-trypsin inhibitor heavy chain H2 precursor (ITI heavy chain H2) (Inter-alpha-inhibitor heavy chain 2) (Inter-alpha-trypsin inhibitor complex component II) (Serum-derived hyaluronan-associated protein) (SHAP)
		Subclass: inter-alpha-trypsin inhibitor family heavy chain-related protein
40	NM_009744. NP_033874.1	F:2.93 (5to19) B-cell lymphoma 6 protein; B-cell CLL/lymphoma-6; cys-his2 zinc finger transcription factor BCL5; zinc finger protein 51; lymphoma-associated zinc finger gene on chromosome 3
		Alternate: similar to Bcl6-associated zinc finger protein
45	NM_017372 NP_059068.1	F:2.91 (7to19) lysozyme
	NM_021313 NP_067288.1	F:2.91 (5to19) RING finger protein 25
50	X93035 CAA63603.1	F:2.87 (YtoO) chitinase
		Subclass: chitinase 3-like 1; cartilage glycoprotein-39
		Subclass: chitotriosidase; plasma methylumbelliferyl tetra-N-acetylchitotetraoside hydrolase
		Subclass: chitinase 3-like 2; chondrocyte protein 39
		Alternate: oviductal glycoprotein
55		Subclass: oviductal glycoprotein 1, 120kDa (mucin 9, oviductin); mucin 9 (oviductin); oviductal glycoprotein 1, 120kD (mucin 9, oviductin)
	NM_023184 NP_075673.1	F:2.87 (5to11) Kruppel-like factor 15; KKLf protein; kidney-enriched Kruppel-like factor
60	NM_010634 NP_034764.1	F:2.84 (5to19) fatty acid binding protein 5 (psoriasis-associated); E-FABP
65	NM_009263 NP_033289.1	F:2.82 (5to19) Osteopontin precursor (Bone sialoprotein 1) (Urinary stone protein) (Secreted phosphoprotein 1) (SPP-1) (Nephropontin) (Uropontin)
		Alternate: OPN-a - human (fragment).
		Alternate: OPN-b - human (fragment).
		Alternate: OPN-c - human (fragment).

5	NM_007779 NP_031805.1	F:2.8 (Sto19)	colony stimulating factor 1 receptor, formerly McDonough feline sarcoma viral (v-fms) oncogene homolog; C-FMS; Colony-stimulating factor-1 receptor; oncogene FMS (McDonough feline sarcoma)
			Alternate: platelet-derived growth factor receptor
			Subclass: platelet-derived growth factor receptor alpha precursor
			Subclass: platelet-derived growth factor receptor beta precursor; beta
			platelet-derived growth factor receptor
			Subclass: platelet-derived growth factor receptor, beta polypeptide
			Subclass: platelet-derived growth factor receptor.
			Alternate: FLT3 receptor tyrosine kinase
			Alternate: fms-related tyrosine kinase 3
10			Alternate: protein-tyrosine kinase (EC 2.7.1.112) STK-1 precursor
15	NM_011825 NP_035955.1	F:2.8 (Sto19)	hypothetical protein FLJ21195 similar to protein related to DAC Alternate: cysteine knot superfamily 1, BMP antagonist 1; gremlin
20	AK007707 BAB25202.1	F:2.79 (Min)	NPD008 protein Alternate: CGI-148 protein
25	NM_026007 NP_080283.1	F:2.76 (YtoM)	eukaryotic translation elongation factor Subclass: eukaryotic translation elongation factor 1 gamma; elongation factor 1-gamma; EF-1-gamma; eEF-1B gamma; translation elongation factor eEF-1 gamma chain; PRO1608; pancreatic tumor-related protein
			Subclass: Similar to eukaryotic translation elongation factor 1 gamma
			Alternate: pancreatic tumor-related protein
			Alternate: PRO1608
30	NM_024169 NP_077131.2	F:2.76 (Sto19)	FK506 binding protein precursor; FK506 binding protein 11 (19 kDa)
35	NM_008061 NP_032087.1	F:2.75 (Sto11)	glucose-6-phosphatase, catalytic
	NM_019806 NP_062780.1	F:2.74 (Sto19)	vesicle-associated membrane protein Subclass: VAMP (vesicle-associated membrane protein)-associated protein B and C; VAMP-associated protein C; VAMP-associated protein B; VAMP-associated 33 kDa protein
			Subclass: vesicle-associated membrane protein (VAMP)-associated protein of 33 kDa; vesicle-associated membrane protein (VAMP), 33 kDa; VAMP-associated protein A; VAMP (vesicle-associated membrane protein)-associated protein A (33kD)
40	NM_022324 NP_071719.1	F:2.74 (Sto19)	stromal cell-derived factor Subclass: stromal cell-derived factor 2-like 1



355

		Subclass: stromal cell-derived factor 2 precursor
		Altname: Unknown (protein for MGC:1757)
5	M12571 AAA57234.1	F:2.73 (YtoM) heat shock protein
		Subclass: Heat shock 70 kDa protein 1 (HSP70.1) (HSP70-1/HSP 70-2)
		Subclass: heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein; dnaK-type molecular chaperone HSP70-1
		Subclass: heat shock 70kDa protein 1-like; Heat-shock 70kD protein-like-1; heat shock 70kD protein-like 1; heat shock 70kD protein 1-like
10		Subclass: heat shock 70kDa protein 1B; heat shock 70kD protein 1B
		Subclass: heat shock 70kDa protein 2; heat shock 70kD protein 2; Heat-shock 70kD protein-2
		Subclass: heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kD protein 10; heat shock cognate protein 5-4; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1
		Subclass: heat shock 70kDa protein 6 (HSP70B')
15	U89415 AAC36522.1	F:2.73 (5to19) eukaryotic translation elongation factor 2; polypeptidyl-tRNA
		Altname: similar to Elongation factor 2 (EF-2)
20	NM_009242 NP_033268.1	F:2.73 (5to19) secreted protein, acidic, cysteine-rich (osteonectin); Osteonectin (secreted protein, acidic, cysteine-rich)
		Altname: SPARC-like protein 1 precursor (High endothelial venule protein) (Hevin) (MAST 9)
		Altname: Unknown (protein for MGC:45264)
25	NM_026104 NP_080380.1	F:2.72 (5to7) similar to RIKEN cDNA 1700095F04
30	AF294617 AAG02118.1	F:2.69 (5to7) 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase
		Subclass: 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3
		Subclass: inducible 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase
		Subclass: 6-phosphofructo-2-kinase heart isoform
		Subclass: 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4
35	NM_007952 NP_031978.1	F:2.65 (5to19) glucose regulated protein, 58kDa; glucose regulated protein, 58kD
		Altname: protein disulfide-isomerase (EC 5.3.4.1) ER60 protein
40	NM_016674 NP_057883.1	F:2.65 (5to19) claudin
		Subclass: claudin 1; senescence-associated epithelial membrane protein 1
		Subclass: claudin 7; Clostridium perfringens enterotoxin receptor-like 2; claudin 9
		Subclass: claudin 19

356

		Subclass: similar to Claudin-19
	NM_008509	F:2.64 (5to19) lipoprotein lipase
5	NP 032535.1	
		Subclass: lipoprotein lipase
		Subclass: Similar to lipoprotein lipase
		Subclass: lipoprotein lipase precursor
		Subclass: endothelial lipase precursor; endothelial cell-derived lipase
10		Subclass: lipase C precursor
		Subclass: hepatic lipase precursor
	NM_009690	F:2.63 (7to19) CD5 antigen-like (scavenger receptor cysteine rich family); Spalpha
	NP 033820.1	
15		Alternate: deleted in malignant brain tumors 1 isoform b precursor
		Alternate: DMBT1/8kb.2 protein
		Alternate: deleted in malignant brain tumors 1 isoform c precursor
		Alternate: deleted in malignant brain tumors 1 isoform a precursor
		Alternate: M130 antigen
20		Alternate: M130 antigen precursor, splice form 1
		Alternate: M130 antigen precursor, splice form 3
		Alternate: CD163 antigen; macrophage-associated antigen
		Alternate: scavenger receptor cysteine-rich type 1 protein M160 precursor
		Alternate: scavenger receptor cysteine rich domain containing, group B (4 domains); scavenger receptor cysteine-rich protein SRCRB-S4D
		Alternate: neurotrypsin precursor; protease, serine, 12; motopsin; brain-specific serine protease 3; leydin
25		
	NM_025459	F:2.63 (7to19) unnamed protein product
	NP 079735.1	
		Alternate: hypothetical protein FLJ20152
30		
	X00496	F:2.63 (5to19) HLA class II histocompatibility antigen, gamma chain (HLA-DR antigens associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD74 antigen)
	CAA25191.1	
		Alternate: hypothetical protein FLJ13902
	NM_011435	F:2.61 (5to19) superoxide dismutase 3, extracellular
35	NP 035565.1	
	NM_007574	F:2.56 (5to19) complement subcomponent C1q chain C
	NP 031600.1	
40		
	AK004387	dynein, axonemal, intermediate polypeptide 1; dynein, axonemal,
	BAC25081.1	F:2.55 (YtoO) intermediate chain 1; dynein intermediate chain DNAT1
	NM_008330	F:2.55 (5to19) hypothetical protein R30953_1
	NP 032087.1	
45		
	NM_009922	
	NP 034052.1	F:2.54 (YtoO) calponin
		Subclass: calponin 1, basic, smooth muscle; calponins, basic; Calponin 1

357

		Subclass: calponin 2; Calonin 2
		Subclass: calponin 3; calponin, acidic
5	NM_010439 NP_034569.1	F:2.52 (5to19) High mobility group protein
		Subclass: high-mobility group box 1; high mobility group box 1; high-mobility group (nonhistone chromosomal) protein 1
		Subclass: dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)
		Subclass: similar to dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)
10		Subclass: High mobility group protein 1-like 10 (HMG-1L10)
		Subclass: high-mobility group box 2; high-mobility group (nonhistone chromosomal) protein 2
		Subclass: high-mobility group box 3; high-mobility group (nonhistone chromosomal) protein 4
		Subclass: nonhistone chromosomal protein HMG-2B - human
		Subclass: similar to High mobility group protein 4 (HMG-4) (High mobility group protein 2a) (HMG-2a)
15		Subclass: HMG2a (high mobility group protein 2a)
		Subclass: similar to HMG2a (high mobility group protein 2a)
		Subclass: SP100-HMG
	X12905 CAA31389.1	F:2.51 (5to19) properdin
20		
	AK007392 BAB25008.1	F:2.49 (5to11) pancreatic elastase
		Subclass: elastase 1, pancreatic
25		Subclass: similar to elastase 1, pancreatic
		Subclass: pancreatic elastase 2 precursor
		Subclass: pancreatic elastase IIB
		Subclass: Elastase IIIB precursor (Protease E)
		Subclass: elastase 3, pancreatic (protease E)
30		Subclass: Elastase IIIA precursor (Protease E)
		Subclass: Similar to elastase 3, pancreatic (protease E)
	NM_016847 NP_058543.1	F:2.48 (5to19) arginine vasopressin receptor
35		Subclass: arginine vasopressin receptor 1A; V1a vasopressin receptor; vascular/hepatic-type arginine vasopressin receptor; antidiuretic hormone receptor 1A
		Subclass: arginine vasopressin receptor 1B; arginine vasopressin receptor 3; antidiuretic hormone receptor 1B; vasopressin V1B receptor; pituitary vasopressin receptor 3
		Subclass: arginine vasopressin receptor 2
		Alternate: oxytocin receptor
40	NM_053177 NP_444407	F:2.47 (7to19) mucolipidin

358

		Subclass: mucolipin 1
		Subclass: mucolipin-3
5	NM_023733 NP_076222.1	F:2.47 (7to19) carnitine O-octanoyltransferase
		Subclass: carnitine O-octanoyltransferase
		Subclass: Peroxisomal carnitine octanoyltransferase (COT)
10	AK007588 XP_135065.1	F:2.47 (5to7) ring finger protein 7; sensitive to apoptosis gene
	NM_019985 NP_064369.1	F:2.46 (7to19) C-type lectin-like receptor-2
15		Alternate: Similar to C-type lectin-like receptor-2
	NM_007572 NP_031598.1	F:2.45 (5to19) complement component 1, q subcomponent, alpha polypeptide precursor; complement C1q A chain precursor; complement component C1q, A chain
20	AF218416 AAF25956.1	F:2.44 (7to19) tocopherol (alpha) transfer protein (ataxia (Friedreich-like) with vitamin E deficiency); Tocopherol (alpha) transfer protein
	NM_019642 NP_062616.1	F:2.41 (YtoM) lchyl-diphosphooligosaccharide--protein glycosyltransferase 63 kDa subunit precursor (Ribophorin II) (RPN-II) (RIBIR)
25		Alternate: Unknown (protein for IMAGE:2961244)
		Alternate: Unknown (protein for IMAGE:3532152)
	NM_010442 NP_034572.1	F:2.41 (7to19) heme oxygenase (decycling)
30		Subclass: heme oxygenase (decycling) 1
		Subclass: heme oxygenase (decycling) 2
	NM_007833 NP_031859.1	F:2.41 (7to19) decorin
35		Subclass: decorin
		Subclass: decorin isoform a preproprotein; dermatan sulphate proteoglycans II; bone proteoglycan II; proteoglycan core protein
		Subclass: decorin isoform b precursor; dermatan sulphate proteoglycans II; bone proteoglycan II; proteoglycan core protein
		Subclass: decorin isoform c precursor; dermatan sulphate proteoglycans II; bone proteoglycan II; proteoglycan core protein
		Alternate: biglycan preproprotein; bone/cartilage proteoglycan-I; dermatan sulphate proteoglycan I
40		Alternate: asporin (LRR class 1); periodontal ligament associated protein 1
	NM_016850 NP_058546.1	F:2.41 (5to19) Interferon regulatory factor 7 (IRF-7)
45		Subclass: interferon regulatory factor 7 isoform b
		Subclass: interferon regulatory factor 7 isoform a
		Subclass: interferon regulatory factor 7 isoform d
		Subclass: putative interferon regulatory factor 7C.2

	NM_009777	F:2.41 (5to19)	complement component 1, q subcomponent, beta polypeptide precursor;
	NP_033907.1		complement component C1q, B chain
5	NM_008524	F:2.41 (5to19)	lumican
	NP_032550.1		
	NM_010789	F:2.4 (5to19)	
10	NP_034919.1		Homeobox protein
			Subclass: TALE homeobox protein Meis2d
			Subclass: Homeobox protein Meis2 (Meis1-related protein 1)
			Subclass: Meis1 homolog; Meis1 (mouse) homolog
			Subclass: TALE homeobox protein Meis2b
			Subclass: TALE homeobox protein Meis2a
15			Subclass: homeobox protein Meis2 isoform c; Meis (mouse) homolog 2;
			Meis1-related gene 1; TALE homeobox protein Meis2
			Subclass: Homeobox protein Meis3 (Meis1-related protein 2)
			Subclass: similar to Homeobox protein Meis3 (Meis1-related protein 2)
			Alternate: Similar to hypothetical protein DKFZp547H236
			Alternate: Unknown (protein for MGC:2820)
20	NM_013485	F:2.38 (5to19)	complement protein
	NP_038513.1		
			Subclass: complement component 9
			Subclass: complement component 8
25	NM_016906	F:2.37 (5to19)	
	NP_058602.1		sec61 homolog
			Subclass: Sec61 alpha form 1; sec61 homolog
			Subclass: Protein transport protein Sec61 alpha subunit isoform 2 (Sec61 alpha-2)
30			Subclass: Similar to Sec61 alpha form 2
			Alternate: Similar to CG9539 gene product
			Alternate: unnamed protein
			Alternate: hypothetical protein
35	AK004979	F:2.37 (5to19)	similar to RIKEN cDNA 1300010M03
	BAB23715.1		
			Alternate: hypothetical protein FLJ20152
			Alternate: unnamed protein product
40	NM_013922		
	NP_038950.1	F:2.36 (7to19)	zinc finger protein KID3
	NM_009369	F:2.36 (5to11)	transforming growth factor, beta-induced, 68kDa; corneal dystrophy; kerato-
45	NP_033395.1		epithelin; transforming growth factor, beta-induced, 68kD
			Alternate: BIGH3
			Alternate: osteoblast specific factor 2 (fasciclin I-like); periostin
	NM_022309	F:2.36 (5to19)	
	NP_071704.1		core-binding factor, beta subunit

360

		Subclass: core-binding factor, beta subunit, isoform 1; polyomavirus enhancer binding protein 2, beta subunit; SL3-3 enhancer factor 1 beta subunit; SL3/AKV core-binding factor beta subunit
		Subclass: core-binding factor, beta subunit, isoform 2; polyomavirus enhancer binding protein 2, beta subunit; SL3-3 enhancer factor 1 beta subunit; SL3/AKV core-binding factor beta subunit
5	AK018585 BAB31292.1	F:2.35 (5to19) hypothetical protein FLJ13373
	NM_013594 NP_038622.1	F:2.35 (5to19) methyl-CpG binding protein
10		Subclass: methyl-CpG binding protein 1
		Subclass: methyl-CpG binding domain protein 1 isoform 1
		Subclass: methyl-CpG binding domain protein 1 isoform 2
		Subclass: methyl-CpG binding protein splice variant 2
		Subclass: methyl-CpG binding domain protein 1 isoform PCM1
15		Subclass: methyl-CpG binding domain protein 1 isoform 3
		Subclass: methyl-CpG binding domain protein 1 isoform 4
	Z35168 CAA84531.1	F:2.34 (YtoM) collagen
		Subclass: alpha 5 type IV collagen, isoform 2, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
20		Subclass: alpha 5 type IV collagen, isoform 1, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
		Subclass: alpha 5 type IV collagen, isoform 3, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
		Subclass: alpha 1 type IV collagen preproprotein; collagen IV, alpha-1 polypeptide; collagen of basement membrane, alpha-1 chain
		Subclass: alpha 2 type IV collagen preproprotein; canstatin
		Subclass: alpha 3 type IV collagen, isoform 1, precursor; collagen IV, alpha-3 polypeptide (goodpasture antigen)
25		Subclass: type IV alpha 6 collagen, isoform B precursor; collagen IV, alpha-6 polypeptide; collagen of basement membrane, alpha-6
		Subclass: alpha 4 type IV collagen precursor; collagen IV, alpha-4 polypeptide; collagen of basement membrane, alpha-4 chain
	NM_010906 NP_035036.1	F:2.34 (YtoM) nuclear factor
30		Nuclear factor 1 X-type (Nuclear factor 1/X) (NF1-X) (NF1-X) (NF-1/X) (CCAAT-box binding transcription factor) (CTF) (TG GCA-binding protein).
		Nuclear factor 1 A-type (Nuclear factor 1/A) (NF1-A) (NF1-A) (NF-1/A) (CCAAT-box binding transcription factor) (CTF) (TG GCA-binding protein).
		Nuclear factor 1 C-type (Nuclear factor 1/C) (NF1-C) (NF1-C) (NF-1/C) (CCAAT-box binding transcription factor) (CTF) (TG GCA-binding protein).
		nuclear factor 1/B

361

5	AK011495	F:2.34 (5to19)	lectin, mannose-binding, 1 precursor; intracellular mannose specific lectin;
	BAB27655.1		endoplasmic reticulum-golgi intermediate compartment protein 53
10	NM_010354	F:2.34 (5to19)	gelsolin (amyloidosis, Finnish type); Gelsolin
	NP_034484.1		
			Alternate: Adseverin (Scinderin)
			Alternate: villin 1; Villin-1
			Alternate: similar to mouse adseverin(D5); similar to PID:g2218019
15			Alternate: KIAA1905 protein
			Alternate: Advillin (p92)
			Alternate: Similar to gelsolin (amyloidosis, Finnish type)
			Alternate: Similar to advillin
20	NM_010238	F:2.33 (7to19)	
	NP_034368.1		bromodomain containing protein
			Subclass: bromodomain containing protein 2; female sterile homeotic-related gene 1 (RING3, KIAA9001)
			Subclass: bromodomain containing protein 3; bromodomain-containing 3; RING3-like gene; open reading frame X
			Subclass: bromodomain-containing protein 4 isoform long; similar to RING3; chromosome-associated protein
25			Subclass: Similar to bromodomain containing 3
	NM_013521	F:2.33 (5to19)	N-formyl peptide receptor
	NP_038549.1		
			Subclass: formyl peptide receptor 1
30			Subclass: formyl peptide receptor-like 1; lipoxin A4 receptor (formyl peptide receptor related)
			Subclass: formyl peptide receptor-like 2
			Subclass: similar to N-formyl peptide receptor-like 2 protein
			Alternate: orphan G-protein coupled receptor Dez isoform a
			Alternate: Chemokine receptor-like 1 (G-protein coupled receptor DEZ) (G protein-coupled receptor ChemR23)
35			Alternate: complement component 5 receptor 1 (C5a ligand); complement component-5 receptor-2 (C5a ligand)
	AK020881		
	BAB32239.1	F:2.32 (YtoM)	utrophin; dystrophin-related protein
40	AF320996	F:2.32 (7to19)	
	AAK73808.1		WW domain-containing adapter with a coiled-coil region
			Subclass: WW domain-containing adapter with a coiled-coil region isoform 1
			Subclass: WW domain-containing adapter with a coiled-coil region, isoform 2
			Subclass: WW domain-containing adapter with a coiled-coil region, isoform 3
			Alternate: hypothetical protein PRO1741
			Alternate: bA48B24.1 (A novel protein containing a formin binding protein

362

		(FBP28) domain)
		Alternate: hypothetical protein
		Alternate: KIAA1844 protein
		Alternate: hypothetical protein MGC10753
45	NM_019830 NP_062804.1	F:2.32 (7to19) methyltransferase
		Subclass: protein arginine N-methyltransferase 1-variant 2
		Subclass: Protein arginine N-methyltransferase 1 (Interferon receptor 1-bound protein 4)
50		Subclass: protein arginine N-methyltransferase 1-variant 1
		Subclass: protein arginine N-methyltransferase 1-variant 3
		Subclass: Protein arginine N-methyltransferase 4
		Subclass: Protein arginine N-methyltransferase 3
		Subclass: HMT1 hnRNP methyltransferase-like 2
55		Subclass: HMT1 hnRNP methyltransferase-like 3
	NM_020564 NP_065589.1	F:2.32 (5to19) sulfotransferase
		Subclass: hydroxysteroid sulfotransferase SULT2B1a
		Subclass: sulfotransferase family, cytosolic, 2B, member 1; sulfotransferase family 2B, member 1
60		Subclass: hydroxysteroid sulfotransferase SULT2B1b
	NM_007614 NP_031640.1	F:2.31 (YtoM) catenin (cadherin-associated protein), beta 1, 88kDa; catenin (cadherin-associated protein), beta 1 (88kD); catenin (cadherin-associated protein), beta 1 (88kDa)
65	NM_010501 NP_034631.1	F:2.3 (YtoM) Interferon-induced protein
		Subclass: interferon-induced protein with tetratricopeptide repeats 4
		Subclass: similar to Interferon-induced protein with tetratricopeptide repeats 4 (IFIT-4) (Interferon-induced 60 kDa protein) (IFI-60K) (ISG-60) (CIG49) (Retinoic acid-induced gene G protein) (RIG-G)
		Subclass: similar to Interferon-induced protein with tetratricopeptide repeats 2 (IFIT-2) (Interferon-induced 54 kDa protein) (IFI-54K) (ISG-54 K)
70		Subclass: interferon-induced protein with tetratricopeptide repeats 1; Interferon, alpha-inducible protein (MW 56kD); interferon-induced protein 56
		Subclass: retinoic acid- and interferon-inducible protein (58kD)
		Alternate: Unknown (protein for MGC: 14710)
	NM_010917 NP_035047.1	F:2.3 (5to11) nidogen (enactin); Nidogen; nidogen (enactin)
75		Subclass: nidogen (enactin)
		Subclass: nidogen 2 (osteonidogen); nidogen 2
		Subclass: Similar to nidogen 2 (osteonidogen)
80	AK005049	F:2.3 (5to19) Carboxypeptidase N 83 kDa chain (Carboxypeptidase N regulatory subunit)



			Alternate: Similar to RIKEN cDNA 1300018K11 gene
5		AK009881 F:2.3 (5to19)	endoplasmic reticulum protein 29 precursor; endoplasmic reticulum luminal protein ERp28
		BAB26559.1	
		NM_009547 F:2.29 (5to7)	zinc finger protein 161 homolog; zinc finger protein homologous to Zfp161 in mouse; (Zinc finger protein 5) (hZF5)
10		NP_033573.1	
		NM_018793 F:2.29 (5to19)	
		NP_061263.1	tyrosine-protein kinase Subclass: IFN-tyk, tyk2=interferon alpha/beta signaling pathway-related protein tyrosine kinase [human, Daudi cell line, Peptide Partial, 899 aa] Subclass: similar to Non-receptor tyrosine-protein kinase TYK2
15			Subclass: tyrosine kinase 2 Subclass: janus kinase 1 Subclass: Janus kinase 2; tyrosine-protein kinase JAK2 Subclass: JAK3_HUMAN; JANUS KINASE 3; JAK-3; LEUKOCYTE JANUS KINASE; L-JAK Subclass: JAK3B
20		NM_018864 F:2.29 (5to19)	
		NP_061352.1	Inositol-1(or 4)-monophosphatase (IMPase) Subclass: Inositol-1(or 4)-monophosphatase (IMPase) (IMP) (Inositol monophosphatase) (Lithium-sensitive myo-inositol monophosphatase A1) Subclass: inositol(myo)-1(or 4)-monophosphatase 2 Subclass: similar to Myo-inositol-1 (or 4)-monophosphatase (IMPase) (IMP) (Inositol monophosphatase) (Lithium-sensitive myo-inositol monophosphatase A1) Subclass: brain myo-inositol monophosphatase A2b; IMPase A2b
25			
		NM_010699 F:2.28 (7to19)	
		NP_034829.1	lactate dehydrogenase Subclass: lactate dehydrogenase A Subclass: Chain A, Human Muscle L-Lactate Dehydrogenase M Chain, Ternary Complex With NADH And Oxamate Subclass: lactate dehydrogenase B Subclass: lactate dehydrogenase C Subclass: lactate dehydrogenase A -like Subclass: similar to lactate dehydrogenase A -like
30			
		NM_010187 F:2.28 (7to19)	IgG Fc receptor
		NP_034317.1	
			Fc-gamma-RIIb2 Fc fragment of IgG, low affinity IIb, receptor for (CD32); Fc fragment of IgG, low affinity II, receptor for (CD32) Fc-gamma-RIIb1
40			
		NM_029813 F:2.28 (5to19)	zinc finger protein
		NP_084089.1	

364

		Subclass: zinc finger protein 14 (KOX 6); GIOT-4 for gonadotropin inducible transcription repressor-4
		Subclass: similar to zinc finger protein 14 (KOX 6); GIOT-4 for gonadotropin inducible transcription repressor-4
		Subclass: similar to zinc finger protein 91 (HPF7, HTF10)
5		Subclass: zinc finger protein 180 (HHZ168)
		Subclass: zinc finger protein 136 (clone pHZ-20)
		Subclass: KIAA1710 protein
		Subclass: similar to Hypothetical zinc finger protein KIAA1710
		Subclass: Zinc finger protein 93 (Zinc finger protein HTF34)
10		Subclass: zinc finger protein 135 (clone pHZ-17)
		Subclass: zinc finger protein 85 (HPF4, HTF1)
		Subclass: KIAA1198 protein
		Subclass: similar to Hypothetical zinc finger protein KIAA1198
		Subclass: similar to Zinc finger protein 135
15		Subclass: similar to Zinc finger protein 93 (Zinc finger protein HTF34)
		Subclass: zinc finger protein 91 (HPF7, HTF10)
		Subclass: zinc finger protein 84 (HPF2)
		Subclass: finger protein 2, placental
		similar to KRAB zinc finger protein KR18
20		Subclass: zinc finger protein A.F020591
		Subclass: kruppel-related zinc finger protein
		Subclass: Similar to zinc finger protein 208
		Subclass: zinc finger protein 71; endothelial zinc finger protein induced by tumor necrosis factor alpha
		Subclass: zinc finger protein 37 homolog (mouse); Zinc finger protein-37, mouse, homolog of; zinc finger protein homologous to Zfp37 in mouse
25		Subclass: zinc finger protein 328
		Subclass: similar to zinc finger protein 29
		Subclass: zinc finger protein 268
		Similar to zinc finger protein 208
		Subclass: Zinc finger protein ZNF45
30		Subclass: zinc finger protein 16 (KOX 9)
		Subclass: similar to Zinc finger protein 85
		Subclass: zinc finger protein 43 (HTF6)
		Subclass: similar to Zinc finger protein 35 (Zfp-35)
		Subclass: zinc finger protein 228
		Subclass: similar to zinc finger protein 20 (Zinc finger protein KOX13) (DKFZp572P0920)
35		Subclass: similar to Zinc finger protein 184
		Subclass: zinc finger protein 177
		Subclass: BB479F17.3 (zinc finger protein 41)
		Subclass: similar to Zinc finger protein 41
		Subclass: zinc finger protein 287
40		Subclass: zinc finger protein 331; zinc finger protein 463; C2H2-like zinc finger protein
		Subclass: zinc finger protein 271
		Subclass: Hypothetical zinc finger protein KIAA1473
		Subclass: similar to Hypothetical zinc finger protein KIAA1473
		Subclass: similar to Hypothetical zinc finger protein KIAA1956
45		Subclass: KRAB zinc finger protein
		Subclass: KIAA1956 protein
		Subclass: TRAF6-inhibitory zinc finger protein; TRAF6-binding zinc finger

365

		protein
		Alternate: hypothetical protein
		Subclass: FLJ40981
50		Subclass: similar to hypothetical protein FLJ40981
		Subclass: hypothetical protein FLJ21628
		Subclass: hypothetical protein FLJ32191
		Subclass: hypothetical protein DKFZp572C163.1
55		Subclass: hypothetical protein FLJ30932
		Subclass: hypothetical protein FLJ14345
		Subclass: hypothetical protein FLJ90396
		Subclass: hypothetical protein FLJ31526
		Subclass: hypothetical protein DKFZp572P0920.1
60	NM_007517 F:2.27 (7to19)	ancient ubiquitous 46 kDa protein AUP1
	NP_031543.1	
		Alternate: AUP1 homolog
65	NM_018816 F:2.27 (5to19)	
	NP_061286.1	Apolipoprotein M (ApoM)
		Alternate: similar to Apolipoprotein M (ApoM) (G3a) (HSPC336)
70	NM_028740 F:2.27 (5to19)	
	NP_083016.1	antichymotrypsin
		Subclass: alpha1-antichymotrypsin
		Subclass: alpha-1-antichymotrypsin precursor
		Subclass: similar to Alpha-1-antichymotrypsin precursor (ACT)
		Subclass: serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3
75	NM_016875	
	NP_058571.1 F:2.26 (YtoO)	germ cell specific Y-box binding protein; contrin
	NM_008362 F:2.26 (5to19)	interleukin 1 receptor, type I precursor; interleukin 1 receptor alpha, type I;
80	NP_032388.1	interleukin receptor 1; antigen CD121a
	NM_008295	
	NP_032321.1 F:2.25 (YtoO)	hydroxysteroid dehydrogenase
		Subclass: hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-
		isomerase 1; Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid
		Subclass: 3-beta-hydroxysteroid dehydrogenase/delta-5-delta-4-isomerase.
85		Subclass: hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-
		isomerase 2; Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid
		Subclass: dJ871G17.4 (novel 3-beta hydroxysteroid
		dehydrogenase/isomerase family member)
		Subclass: 3 beta-hydroxy-delta 5-C27-steroid oxidoreductase
90	NM_008340 F:2.25 (7to19)	insulin-like growth factor binding protein, acid labile subunit; INSULIN-
	NP_032366.1	LIKE GROWTH FACTOR BINDING PROTEIN COMPLEX ACID
		LABILE CHAIN PRECURSOR
	NM_008343 F:2.25 (5to11)	insulin-like growth factor binding protein 3

366

5	NP_032369.1		Alternate: insulin-like growth factor binding protein 5
	NM_008929	F:2.25 (5to19)	interferon-induced double-stranded RNA-activated protein kinase inhibitor
	NP_032955.1		
10	NM_013585	F:2.25 (5to19)	proteasome endopeptidase complex
	NP_038613.1		Subclass: proteasome beta 9 subunit isoform 1 proprotein; proteasome subunit, beta type, 9; proteasome-related gene 2; proteasome chain 7; macropain chain 7; low molecular mass protein 2; multicatalytic endopeptidase complex chain 7; proteasome catalytic subunit 1i; proteasome subunit beta 6i
			Subclass: proteasome beta 9 subunit isoform 2 proprotein; proteasome subunit, beta type, 9; proteasome-related gene 2; proteasome chain 7; macropain chain 7; low molecular mass protein 2; multicatalytic endopeptidase complex chain 7; proteasome catalytic subunit 1i; proteasome subunit beta 6i
15	NM_008035	F:2.24 (YtoO)	folate-binding protein
	NP_032061.1		Subclass: folate binding protein 2
			Subclass: folate receptor 3 precursor
20			Subclass: folate receptor 1 (adult)
			Subclass: similar to Folate receptor gamma precursor (FR-gamma) (Folate receptor 3)
	NM_025649		gene predicted from cDNA with a complete coding sequence; caught by
25	NP_079925.1	F:2.24 (Min)	MAD Two 2
	NM_011656	F:2.24	tuftelin 1
	NP_035786.1	(11to19)	Alternate: Similar to tuftelin 1
30			Alternate: unnamed protein product
	NM_021099		
	NP_066922.1	F:2.23 (YtoO)	protein kinase transmembrane receptor
35			Subclass: KIT protein
			Subclass: colony stimulating factor receptor
			Subclass: platelet-derived growth factor receptor
40			Subclass: FLT3 receptor tyrosine kinase
			Subclass: vascular endothelial growth factor receptor
			Subclass: fibroblast growth factor receptor
40			Subclass: ret proto-oncogene
	NM_008290		
	NP_032316.1	F:2.23 (YtoO)	hydroxysteroid dehydrogenase
			Subclass: hydroxysteroid (17-beta) dehydrogenase 2
			Subclass: 11beta-hydroxysteroid dehydrogenase (EC 1.1.1.146) type 2

	NM_008180	F:2.23 (5to19)	glutathione synthetase
	NP_032206.1		
5	NM_007468	F:2.22 (7to11)	
	NP_031494.1		apolipoprotein
			Subclass: apolipoprotein A-IV
			Subclass: Apolipoprotein A-IV precursor (Apo-AIV)
10	NM_007489	F:2.22 (7to11)	
	NP_031515.1		receptor nuclear translocator/transcription factor
			Subclass: aryl hydrocarbon receptor nuclear translocator-like
			Subclass: aryl hydrocarbon receptor nuclear translocator; Amt
			Subclass: Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2)
			Subclass: PAS protein 3
15			Subclass: BMAL1 protein (Brain and muscle ARNT-like 1) (Member of PAS protein 3) (Basic-helix-loop-helix-PAS orphan MOP3) (BHLH-PAS protein JAP3)
			Subclass: transcription factor BMAL2
			Subclass: brain-muscle-ARNT-like transcription factor 2a
			Subclass: brain-muscle-ARNT-like transcription factor 2b
			Subclass: brain-muscle-ARNT-like transcription factor 2c
20			Subclass: brain-muscle-ARNT-like transcription factor 2d
			Subclass: bHLH-PAS transcription factor MOP9
			Subclass: bHLH-PAS transcription factor MOP9
			Subclass: Similar to transcription factor BMAL2
			Subclass: brain and muscle Ah receptor nuclear translocator-like protein, BMAL1e
25			Subclass: brain and muscle Ah receptor nuclear translocator-like protein, BMAL1d
	NM_022985	F:2.22 (7to19)	protein associated with PRK1; hypothetical protein; associated with PRK1
	NP_075361.2		
30			Alternate: hypothetical protein
			Alternate: zinc finger protein 216
			Alternate: similar to protein associated with PRK1; hypothetical protein; associated with PRK1
	NM_018754	F:2.22 (5to7)	stratifin
	NP_061224.1		
35			Alternate: Similar to stratifin
			Alternate: tyrosine 3/tryptophan 5-monooxygenase activation protein
			Subclass: tyrosine 3/tryptophan 5-monooxygenase activation protein, zeta polypeptide; protein kinase C inhibitor protein-1; phospholipase A2
			Subclass: tyrosine 3/tryptophan 5-monooxygenase activation protein, theta polypeptide; 14-3-3 protein tau
			Subclass: tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide; 14-3-3 protein beta/alpha; Protein kinase C inhibitor protein-1; Protein 1054

368

		Subclass: tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide
		Subclass: tyrosine 3/tryptophan 5-monooxygenase activation protein, eta polypeptide
5	NM_007825 NP_031851.1	F:2.22 (5to19) cytochrome P450, subfamily VIIb, polypeptide 1; oxysterol 7alpha-hydroxylase
		Alternate: Cytochrome P450 7A1 (Cholesterol 7-alpha-monooxygenase) (CYPVII) (Cholesterol 7-alpha-hydroxylase)
10	NM_021354 NP_067329.1	F:2.21 (7to19) developmentally regulated GTP binding protein
		Subclass: developmentally regulated GTP binding protein 2
		Subclass: developmentally regulated GTP binding protein 1; neural precursor cell expressed, developmentally down-regulated 3;
		developmentally regulated GTP-binding protein 1
15	NM_007912 NP_031938.1	F:2.21 (5to19) Epidermal growth factor receptor
		Subclass: epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian); epidermal growth factor receptor (avian erythroblastic leukemia viral (v-erb-b) oncogene homolog); Epidermal growth factor receptor
		Subclass: p110 epidermal growth factor receptor
		Subclass: v-erb-a erythroblastic leukemia viral oncogene homolog 4; avian erythroblastic leukemia viral (v-erb-b2) oncogene homolog 4; v-erb-a avian erythroblastic leukemia viral oncogene homolog-like 4
		Subclass: v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian); Transformation gene ERBB-3; v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3
20		Subclass: Receptor protein-tyrosine kinase erbB-3 (c-erbB3) (Tyrosine kinase-type cell surface receptor HER3)
		Subclass: v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog; Avian erythroblastic leukemia viral (v-erb-b2) oncogene homolog 2; v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2 (neuro/glioblastoma derived oncogene homolog)
		Subclass: Similar to v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3
		Subclass: herstatin
25	NM_021522 NP_067497.1	F:2.21 (5to19) ubiquitin specific protease 14
	NM_007711 NP_031737.1	F:2.2 (YtoM) chloride channel protein

369

			Subclass: Chloride channel protein 3 (CIC-3).
			Subclass: Chloride channel protein 4 (CIC-4).
			Subclass: chloride channel 5; Chloride channel-5
5	NM_008245 NP_032271.1	F:2.2 (7to19)	hematopoietically expressed homeobox; proline-rich homeodomain-containing transcription factor
			Alternate: Similar to hematopoietically expressed homeobox
			Alternate: meobox related protein
10	AK003121 BAB22581.1	F:2.2 (5to19)	hypothetical protein MGC3279 similar to collectins
			Alternate: collectin sub-family member 10; collectin liver 1; collectin 34
15	NM_016704 NP_057913.1	F:2.2 (5to19)	complement component
			Subclass: complement component C6
			Subclass: Complement component 6 precursor
			Subclass: similar to Complement component C6 precursor
			Subclass: complement C7
20			Subclass: complement component 7 precursor
	NM_021525 NP_067500.1	F:2.19 (7to19)	RNA cyclase
25			Subclass: RNA cyclase homolog
			Subclass: Similar to RNA cyclase homolog
			Subclass: RNA 3'-terminal phosphate cyclase-like protein
			Alternate: HSPC338
30	NM_022434 NP_071879.1	F:2.19 (5to19)	cytochrome P-450
			Subclass: cytochrome P450, subfamily IVF, polypeptide 2; leukotriene B4 omega-hydroxylase; leukotriene-B4 20-
			Subclass: cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega; alkane-1 monooxygenase; lauric acid omega-hydroxylase
			Subclass: cytochrome P450, subfamily IVF, polypeptide 11
35			Subclass: cytochrome P450 4F2
			Subclass: cytochrome P450, subfamily IVF, polypeptide 3; leukotriene B4 omega hydroxylase; leukotriene-B4 20-monoxygenase; cytochrome P450-LTB-omega
			Subclass: Cytochrome P450 4F12 (CYPIVF12)
			Subclass: similar to Cytochrome P450 4F12 (CYPIVF12)
			Subclass: cytochrome P450, subfamily IVF, polypeptide 8; microsomal monooxygenase; flavoprotein-linked monooxygenase
40			Subclass: similar to CYTOCHROME P450 4F6 (CYPIVF6)
			Alternate: hypothetical protein
			Alternate: F22329_1
			Alternate: Q9FHB6
45	NM_007899 NP_031925.1	F:2.18 (5to11)	extracellular matrix protein 1

370

		Subclass: extracellular matrix protein 1, isoform 1 precursor; secretory component p85
		Subclass: extracellular matrix protein 1, isoform 2 precursor; secretory component p85
5	NM_010028 NP_034158.1	F:2.18 (5to19) DEAD-box protein
		Subclass: DEAD-box protein 3 (Helicase-like protein 2) (HLP2) (DEAD-box, X isoform)
		Subclass: DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3; DEAD/H box-3; helicase like protein 2; CAP-Rf
		Subclass: DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 4; VASA protein
		Subclass: probable RNA helicase protein DKFZp434B1122.1
10		Subclass: similar to DEAD (aspartate-glutamate-alanine-aspartate) box polypeptide 3; D-E-A-D (aspartate-glutamate-alanine-aspartate) box polypeptide 3; embryonic RNA helicase
		Subclass: DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 17 isoform 1; DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 17 (72kD); probable RNA-dependent helicase p72
		Alternate: growth regulated nuclear 68 protein
15	NM_053215 NP_444445.1	F:2.18 (5to19) UDP glycosyltransferase; UDP-glucuronyltransferase
		Subclass: UDP glycosyltransferase 2 family, polypeptide B17; UDP-glucuronyltransferase, family 2, beta-17
		Subclass: similar to UDP-glucuronosyltransferase 2B15 precursor, microsomal (UDPGT) (UDPGTH-3) (HLUG4)
		Subclass: UDP glycosyltransferase 2 family, polypeptide B15; UDP-glucuronyltransferase, family 2, beta-15
		Subclass: UDP glycosyltransferase 2 family, polypeptide B4; UDP-glucuronyltransferase, family 2, beta-4
20		Subclass: similar to UDP-glucuronosyltransferase 2B4 precursor, microsomal (UDPGT) (Hydroxycholeic acid) (HLUG25) (UDPGTH-1)
		Subclass: UDP glycosyltransferase 2 family, polypeptide B7; UDP-glucuronyltransferase, family 2, beta-7
		Subclass: UDP glycosyltransferase 2 family, polypeptide A1; UDP-glucuronosyltransferase 2 family, polypeptide A1
		Subclass: UDP glycosyltransferase 2 family, polypeptide B11
25		Subclass: UDP glycosyltransferase 2 family, polypeptide B10
		Subclass: UDP glycosyltransferase 2 family, polypeptide B28
	NM_015784 NP_056599.1	F:2.17 (YtoO) osteoblast specific factor 2 (fascin I-like); periostin
30	AK007710 BAB25204.1	F:2.17 (5to19) hypothetical protein FLJ12150
		Alternate: FKSG10



NM_011415	F:2.16 (5to11)	snail 2; neural crest transcription factor SLUG; slug (chicken homolog), zinc
NP_035545.1		finger protein
		Alternate: snail 1 homolog; snail 1 zinc finger protein
		Alternate: similar to snail 1 (drosophila homolog), zinc finger protein
AK011306	F:2.16 (5to19)	
BAB27532.1		eukaryotic translation initiation factor
		Subclass: eukaryotic translation initiation factor 5A; eIF5A1; eIF5A
		Subclass: similar to eukaryotic initiation factor 5A
		Subclass: eIF-5A2 protein; eIF5AII
NM_007686	F:2.16 (5to19)	Complement factor
NP_031712.1		Subclass: Complement factor I
		Subclass: Complement factor I precursor (C3B/C4B inactivator)
		Subclass: Similar to I factor (complement)
NM_010378	F:2.15	MHC class II antigen alpha chain
NP_034508.1	(11to19)	
		Subclass: MHC class II histocompatibility antigen HLA-DC-4 alpha chain precursor
		Subclass: MHC class II histocompatibility antigen HLA-DQ alpha 1 (DQw4 specificity) precursor
		Subclass: HLA class II histocompatibility antigen, DQ(2) alpha chain
		Subclass: HLA class II histocompatibility antigen, DQ(5) alpha chain precursor (DC-1 alpha chain)
		Subclass: MHC HLA-DX-alpha chain
		HLA class II histocompatibility antigen, DQ(W3) alpha chain precursor
		Subclass: similar to HLA class II histocompatibility antigen, DQ(3) alpha chain precursor (DC-alpha) (HLA-DCA) (HLA-DQA1*05011)
		Subclass: similar to HLA class II histocompatibility antigen, DP alpha chain precursor (HLA-SB alpha chain) (MHC class II DP3-alpha) (DP(W3)) (DP(W4))
		Subclass: major histocompatibility complex, class II, DO alpha; lymphocyte antigen; HLA-D0-alpha; major histocompatibility complex, class II, DN alpha
		Subclass: major histocompatibility complex, class II, DR alpha precursor; HLA class II histocompatibility antigen, DR alpha chain
AK008273	F:2.15 (7to19)	Rho GDP dissociation inhibitor (GDI)
XP_132918.1		Subclass: Rho GDP dissociation inhibitor (GDI) beta; Ly-GDI
		Subclass: Rho GDP dissociation inhibitor (GDI) alpha
		Alternate: Ras-Related C3 Botulinum Toxin Substrate 2
AK018195	F:2.15 (5to19)	dynamin 1-like protein
BAC38054.1		Subclass: dynamin 1-like protein, isoform 1; dynamin-like protein

372

5

10

15

20

25

30

35

		Subclass: dynamin 1-like protein, isoform 2; dynamin-like protein
		Subclass: dynamin 1-like protein, isoform 3; dynamin-like protein
		Subclass: Dnm1p/Vps1p-like protein
		Subclass: dynamin-like protein DYNIV-11
		Subclass: Similar to dynamin 1-like
		Subclass: dynamin, internal form 1, long C-terminal form
		Subclass: dynamin, internal form 2, short C-terminal form
		Subclass: Dynamin 2
		Subclass: dynamin 2; Dynamin II
		Subclass: similar to Dynamin 3 (Dynamin, testicular) (T-dynamin)
		Subclass: bA277C14.1 (novel Dynamin family member (KIAA0820))
		Alternate: KIAA0820 protein
NM_013562	F:2.15 (5to19)	
NP_038590.1		INTERFERON-RELATED DEVELOPMENTAL REGULATOR
		Subclass: INTERFERON-RELATED DEVELOPMENTAL REGULATOR 1 (NERVE GROWTH FACTOR-INDUCIBLE PROTEIN PC4)
		Subclass: similar to INTERFERON-RELATED DEVELOPMENTAL REGULATOR 1 (NERVE GROWTH FACTOR-INDUCIBLE PROTEIN PC4)
		Subclass: Interferon-related developmental regulator 2 (SKMC15 protein)
NM_008015	F:2.14 (5to19)	DEAD box RNA helicase
NP_032041.1		Subclass: DEAD box RNA helicase DDX3
		Subclass: dead box, X isoform
		Subclass: DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide, Y chromosome; DEAD/H box-3, Y-linked
		Subclass: similar to DEAD (aspartate-glutamate-alanine-aspartate) box polypeptide 3; D-E-A-D (aspartate-glutamate-alanine-aspartate) box polypeptide 3; embryonic RNA helicase
		Alternate: VASA protein
		Alternate: hypothetical protein
AK008590	F:2.14 (5to19)	
BAB25764.1		Ectonucleoside triphosphate diphosphohydrolase
		Subclass: Ectonucleoside triphosphate diphosphohydrolase 1 (NTPDase1) (Ecto-ATP diphosphohydrolase) (ATPDase) (Lymphoid cell activation antigen) (Ecto-apyrase) (CD39 antigen)
		Subclass: Ectonucleoside triphosphate diphosphohydrolase 2 (NTPDase2) (Ecto-ATPase) (CD39 antigen-like 1)
		Subclass: ectonucleoside triphosphate diphosphohydrolase 3; CD39-like 3
		Subclass: E-type ATPase
NM_009895		
NP_034025.1	F:2.13 (Min)	cytokine-inducible SH2-containing protein
		Subclass: cytokine-inducible SH2-containing protein isoform 2; cytokine-inducible SH2-containing protein; cytokine-inducible inhibitor of signaling type 1B; suppressor of cytokine signaling

373

		Subclass: cytokine-inducible SH2-containing protein isoform 1; cytokine-inducible SH2-containing protein; cytokine-inducible inhibitor of signaling type 1B; suppressor of cytokine signaling
5	NM_025774 NP_080050.1	F:2.13 (5to11) hypothetical protein FLJ13902
	NM_019775 NP_062749.1	F:2.13 (5to19) plasma carboxypeptidase B
		Subclass: plasma carboxypeptidase B2 isoform a preproprotein; thrombin-activatable fibrinolysis inhibitor; thrombin-activable fibrinolysis inhibitor; carboxypeptidase U; carboxypeptidase B-like protein; procarboxypeptidase U; procarboxypeptidase R; plasma procarboxypeptidase B
10		Subclass: plasma carboxypeptidase B2 isoform b; thrombin-activable fibrinolysis inhibitor; thrombin-activatable fibrinolysis inhibitor; carboxypeptidase U; carboxypeptidase B-like protein; procarboxypeptidase U; procarboxypeptidase R; plasma procarboxypeptidase B
		Subclass: carboxypeptidase B-like protein
	NM_008348 NP_032374.1	F:2.12 (YtoO) interleukin 10 receptor, alpha
15	NM_020590 NP_065615.1	F:2.12 (7to19) GABA(A) receptor-associated protein
		Subclass: GABA(A) receptor-associated protein like 1; early estrogen-regulated protein
		Subclass: GABA(A) receptors associated protein like 3
20	NM_011375 NP_035505.1	F:2.12 (5to19) sialyltransferase
		Subclass: sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase); ganglioside G(M3) Synthase
		Subclass: sialyltransferase 6 isoform j; Gal beta-1,3(4)GlcNAc alpha-2,3-sialyltransferase; CMP-N-acetylneuraminatate-beta-1,4-galactoside alpha-2,3-sialyltransferase; alpha-2,3-sialyltransferase II; alpha 2,3-sialyltransferase III
25	NM_013563 NP_038591.1	F:2.11 (YtoO) interleukin 2 receptor, gamma chain, precursor; Interleukin-2 receptor, gamma; common cytokine receptor gamma chain; CD132
	NM_021291 NP_067266.1	F:2.11 (YtoM) amino acid transporter
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 9; solute carrier family 7, member 9; solute carrier family 7 (cationic amino acid, transporter, y+ system), member 9
30		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 5; Membrane protein E16; Solute carrier family 7, member

		5; 4F2 light chain
		Subclass: solute carrier family 7, (cationic amino acid transporter, y+ system) member 11; cystine/glutamate transporter
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 7
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 6
35		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 8
		Subclass: Y+L amino acid transporter 1 (y(+)-L-type amino acid transporter 1) (y+LAT-1) (Y+LAT1) (Monocyte amino acid permease 2) (MOP-2).
		Subclass: solute carrier family 7, member 10; asc-type amino acid transporter 1
		Subclass: Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2).
40	NM_010016 NP_034146.1	F:2.11 (7to11) decay-acceleration factor
		Subclass: decay accelerating factor for complement (CD55, Crmer blood group system); Decay-accelerating factor of
		Subclass: decay-accelerating factor, splice form 1 precursor
45		Subclass: decay-accelerating factor 1 ab
		Subclass: decay-accelerating factor 4ab
		Subclass: decay-accelerating factor 3
	L16846 AAA37327.1	F:2.11 (7to19) B-cell translocation protein; Subclass: B-cell translocation protein 1
50		Subclass: BTG family, member 2; B-cell translocation gene 2 (pheochromocytoma cell-3); B-cell translocation gene 2
	NM_022310 NP_071705.1	F:2.11 (7to19) Heat shock protein
		Subclass: heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa); BiP; heat shock 70kD protein 5 (glucose-regulated protein, 78kD); Heat-shock 70kD protein-5 (glucose-regulated protein, 78kD)
55		Subclass: similar to 78 kDa glucose-regulated protein precursor (GRP 78) (Immunoglobulin heavy chain binding protein) (BIP) (Endoplasmic reticulum luminal Ca2+ binding protein grp78)
		Subclass: heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kd protein 10; heat shock cognate protein 54; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1
		Subclass: Heat shock 70 kDa protein 1 (HSP70.1) (HSP70-1/HSP70-2)
		Subclass: heat shock 70kDa protein 1-like; Heat-shock 70kD protein-like-1; heat shock 70kD protein-like 1; heat shock 70kD protein 1-like
		Subclass: heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein; dnaK-type molecular chaperone HSP 70-1

375

		Subclass: heat shock 70kDa protein 1B; heat shock 70kD protein 1B
		Subclass: heat shock 70kDa protein 2; heat shock 70kD protein 2; Heat-shock 70kD protein-2
		Subclass: heat shock cognate protein 54
		Subclass: heat shock 70kDa protein 9B (mortalin-2); heat shock 70kD protein 9 (mortalin); mot-2; mthsp75; heat shock 70kD protein 9B (mortalin-2); Heat-shock 70kD protein-9 (mortalin)
5		Subclass: heat shock 70kDa protein 6 (HSP70B'); heat shock 70kD protein 6 (HSP70B'); Heat-shock 70kD protein-6 (HSP70B')
		Subclass: Similar to heat shock cognate 71-kd protein
		Subclass: dnaK-type molecular chaperone HSPA1L
		Alternate: Unknown (protein for MGC:33922)
10	AK004654 BAB23445.1	F:2.11 (5to7) Similar to hypothetical protein FLJ13511
		Alternate: F02569_2
		Alternate: 7h3 protein
15	AK009563 BAB26361.1	F:2.1 (5to19) Protein KIAA1434
		Alternate: similar to KIAA1434 protein
		Alternate: unnamed protein product
20	NM_011579 NP_035709.1	F:2.1 (5to19) hypothetical protein R30953_1
	NM_021394 NP_067369.1	F:2.1 (5to19) dJ718J7.3.1 (novel protein similar to mouse tumour stroma and activated macrophage protein DLM-1, isoform 1)
25		Alternate: tumor stroma and activated macrophage protein DLM-1; chromosome 20 open reading frame 183
	NM_016702 NP_057911.1	F:2.1 (5to19) alanine-glyoxylate aminotransferase; alanine-glyoxylate aminotransferase, liver-specific peroxisomal; serine-pyruvate aminotransferase
30	NM_013550 NP_038578.1	F:2.09 (YtoO) H4 histone family, member A
	AK003938 BAB23084.1	F:2.09 (YtoM) KIAA1866 protein
35		
	NM_019571 NP_062517.1	F:2.09 (YtoM) tetraspan 5; tetraspan TM4SF; tetraspan NET-4; transmembrane 4 superfamily member 9; transmembrane 4 superfamily, member 8; tetraspanin 5
40	NM_007509 NP_031535.2	F:2.09 (7to19) ATPase
		Subclass: ATPase, H+ transporting, lysosomal 56/58kD, V1 subunit B, isoform 2; vacuolar proton pump B isoform 2; endomembrane proton pump

376

		58 kDa subunit; vacuolar ATP synthase subunit B, brain isoform; V-ATPase B2 subunit; H(+)-transporting two-sector ATPase, 56/58kD subunit, isoform 2
		Subclass: ATPase, H+ transporting, lysosomal 56/58kD, V1 subunit B, isoform 1; ATPase, H+ transporting, lysosomal, beta polypeptide, 58kD; vacuolar proton pump, subunit 3; vacuolar ATP synthase subunit B, kidney isoform; V-ATPase B1 subunit; endomembrane proton pump 58 kDa subunit; H(+)-transporting two-sector ATPase, 58kD subunit; H+-ATPase beta 1 subunit; ATPase, H+ transporting, lysosomal 56/58kD, V1 subunit B, isoform 1 (Renal tubular acidosis with deafness)
45		Alternate: Unknown (protein for IMAGE:3352651)
		Alternate: Unknown (protein for MGC:32642)
	NM_008932 NP_032958.1	prolactin receptor
50		Subclass: prolactin receptor
		Subclass: prolactin receptor short isoform 1a
		Subclass: intermediate prolactin receptor isoform
		Subclass: prolactin receptor short isoform 1b
		Subclass: delta 4-SF1b truncated prolactin receptor
55		Subclass: prolactin receptor isoform delta S1 precursor
		Subclass: delta 4-delta 7/11 truncated prolactin receptor
	AK003950 BAB23088.1	Similar to RIKEN cDNA 1110029A09 gene
60		Alternate: unnamed protein product
	AK010325 NP_542123.1	transmembrane protein 9 superfamily
		Subclass: transmembrane 9 superfamily member 1; multi-spanning membrane protein (70kD); transmembrane protein 9 superfamily member 1
		Subclass: transmembrane 9 superfamily member 2; 76 kDa membrane protein; transmembrane protein 9 superfamily member 2
65		Subclass: transmembrane protein TM9SF3
		Subclass: similar to Transmembrane 9 superfamily protein member 3 precursor (SM-11044 binding protein) (EP70-P-iso)
		Alternate: KIAA0255 gene product
		Alternate: SM-11044 binding protein
70		Alternate: unnamed protein product
	NM_011521 NP_035651.1	Syndecan-4 precursor (Amphiglycan) (SYND4) (Ryudocara core protein)
	NM_019437 NP_062310.1	hypothetical protein FLJ11149
75		Alternate: unnamed protein product
	NM_007811 NP_031837.1	Cytochrome P450 26 (Retinoic acid-metabolizing cytochrome) (P450RAI) (hP450RAI) (Retinoic acid 4-hydroxylase)

	NM_010324	F:2.08 (5to11)
	NP_034454.1	transaminase
		Subclass: aspartate aminotransferase 1; glutamic-oxaloacetic transaminase 1, soluble
5		Subclass: glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)
	NM_008364	F:2.08 (5to19)
	NP_032390.1	interleukin 1 receptor accessory protein
		Subclass: interleukin 1 receptor accessory protein isoform 1
10		Subclass: interleukin 1 receptor accessory protein isoform 2
		Subclass: interleukin 1 receptor accessory protein-like 2; interleukin 1 receptor 9; IL-1 receptor; X-linked interleukin-1 receptor accessory protein-like 2; IL-1 receptor accessory protein-like 2
	NM_023580	F:2.08 (5to19)
	NP_076069.1	receptor protein-tyrosine kinase
15		Subclass: EphA1; eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence; oncogene EPH; ephrin receptor EphA1); eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence); ephrin receptor EphA1
		Subclass: EphA2; ephrin receptor EphA2; epithelial cell receptor protein tyrosine kinase
		Subclass: EphA7; Hek1; ephrin receptor EphA7
		Subclass: EphA4; Hek8; TYRO1 protein tyrosine kinase; ephrin receptor EphA4
		Subclass: Ephrin type-A receptor 5 precursor (Tyrosine-protein kinase receptor EHK-1) (Eph homology kinase-1) (Receptor protein-tyrosine kinase HEK7)
20		Subclass: similar to Ephrin type-A receptor 5 precursor (Tyrosine-protein kinase receptor EHK-1) (Eph homology kinase-1) (Receptor protein-tyrosine kinase HEK7)
		Subclass: EphA3; Ephrin receptor EphA3 (human embryo kinase 1); eph-like tyrosine kinase 1 (human embryo kinase 1); ephrin receptor EphA3
		Subclass: ephrin receptor EphA8 precursor; ephrin type-A receptor 8 precursor; eph- and elk-related tyrosine kinase; tyrosylprotein kinase; tyrosine-protein kinase receptor eek; protein-tyrosine kinase; hydroxyaryl-protein kinase
		Subclass: ephrin receptor EphB6 precursor; tyrosine-protein kinase-defective receptor; ephrin type-B receptor 6
		Subclass: ephrin receptor EPHA3 secreted form
25		Subclass: large erk kinase
		Subclass: dJ74M1.1.1 (tyrosine kinase isoform 1)
		Subclass: dJ74M1.1.2 (tyrosine kinase isoform 2)
		Alternate: KIAA1459 protein

	AK004731		
	XP 148015	F:2.07 (YtoM)	plakophilin
			Subclass: plakophilin 2
5			Subclass: plakophilin 2a
	NM_008961	F:2.07 (7to19)	phosphotriesterase related; resiniferatoxin-binding, phosphotriesterase-related gene; phosphotriesterase-related
	NP 032987.1		
	NM_025448	F:2.07 (7to19)	signal sequence receptor, beta (translocon-associated protein beta)
10	NP 079724.1		
	L27439	F:2.07 (5to19)	protein S (alpha); Protein S, alpha
	AAA40006.1		Alternate: growth arrest-specific 6; AXL stimulatory factor
15			
	M12573	F:2.07 (5to19)	heat shock 70kDa protein
	AAA37863.1		
			Subclass: heat shock 70kDa protein 1A; heat shock 70kD protein 1A; heat shock-induced protein; dnaK-type molecular chaperone HSP70-1
			Subclass: heat shock 70kDa protein 1B; heat shock 70kD protein 1B
20			Subclass: heat shock 70kD protein 1-like
			Subclass: heat shock 70kDa protein 6 (HSP70B)
			Subclass: heat shock 70kDa protein 2; heat shock 70kD protein 2; Heat-shock 70kD protein-2
			Subclass: heat shock 70kDa protein 8 isoform 1; heat shock cognate protein, 71-kDa; heat shock 70kD protein 10; heat shock cognate protein 54; constitutive heat shock protein 70; lipopolysaccharide-associated protein 1; LPS-associated protein 1
			Subclass: Similar to heat shock 70kD protein 8
25			Subclass: similar to HEAT SHOCK 70 KD PROTEIN 6 (HEAT SHOCK 70 KD PROTEIN B)
	NM_009780	F:2.07 (5to19)	complement component
	NP 033910.1		
			Subclass: complement component C4
30			Subclass: complement component C4A
			Subclass: complement component 4A preproprotein; acidic C4; Rodgers form of C4; complement component 4S
			Subclass: complement component 4B preproprotein; Chido form of C4; basic C4; complement component 4F
			Subclass: complement component C4B
			Subclass: complement C4d
35			Subclass: complement C4d variant
			Subclass: complement component 3
			Subclass: complement component 5
	U27315	F:2.07 (5to19)	
40	AACS2837.1		solute carrier family (mitochondrial carrier; adenine nucleotide translocator)
			Subclass: solute carrier family 25 (mitochondrial carrier; adenine nucleotide



379

		translocator), member 4; adenine nucleotide translocator 1
		Subclass: similar to ADP,ATP carrier protein, heart/skeletal muscle isoform T1 (ADP/ATP translocase 1) (Adenine nucleotide translocator 1) (ANT1)
		Subclass: solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5; 2F1; adenine nucleotide translocator 2
		Subclass: ADP/ATP carrier protein (adenine nucleotide translocator 2)
45		Subclass: similar to ADP,ATP carrier protein, fibroblast isoform (ADP/ATP translocase 2) (Adenine nucleotide translocator 2) (ANT 2)
		Subclass: similar to ADP,ATP carrier protein, liver isoform T2 (ADP/ATP translocase 3) (Adenine nucleotide translocator 3) (ANT 3)
		Subclass: Similar to solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5
		Alternate: hypothetical protein DKFZp434N1235
50	NM_007860 NP_031886.1	F:2.O6 (7to19) Type I iodothyronine deiodinase (Type-I 5'deiodinase) (DIO1) (Type 1 DI) (SDI)
		Alternate: Similar to deiodinase, iodothyronine, type I
	NM_020001 NP_064385.1	F:2.O6 (5to19) dendritic cell lectin b; blood dendritic cell antigen 2 protein
55		
	NM_026533 NP_080809.1	F:2.O6 (5to19) ribosomal protein S13; 40S ribosomal protein S13
60	NM_033373 NP_203537.1	F:2.O5 (YtoO) keratin
		Subclass: keratin 23 isoform a; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cytokeratin 23; type I intermediate filament cytokeratin; histone deacetylase inducible keratin 23, (Cytokeratin 23) (K23) (CK 23).
		Subclass: keratin 23 isoform b; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cytokeratin 23; type I intermediate filament cytokeratin; histone deacetylase inducible keratin 23
		Subclass: keratin 20, type I-like, cytoskeletal
		Subclass: keratin 19; keratin, type I cytoskeletal 19; keratin, type I, 40-kd; cytokeratin 19; (Cytokeratin 19) (K19) (CK 19).
65		Subclass: keratin 17
		Subclass: keratin 12 (Meesmann corneal dystrophy); Keratin-12; keratin 12
		Subclass: keratin 15; keratin-15, basic; keratin-15, beta; type I cytoskeletal 15; cytokeratin 15; (Cytokeratin 15) (K15) (CK 15).
		Subclass: keratin 13; keratin, type I cytoskeletal 13; cytokeratin 13
70		Subclass: keratin 16; keratin, type I cytoskeletal 16; cytokeratin 16
		Subclass: keratin 14; cytokeratin 14
		Subclass: type I hair keratin 6; keratin, hair, acidic, 6
		Subclass: cytokeratin 20
		Subclass: type I hair keratin 5; Ha-5; hard keratin, type I, 5
75		Subclass: Keratin, type I cytoskeletal 10 (Cytokeratin 10) (K10) (CK 10).
		Subclass: type I hair keratin 3A; Ha-3i; hard keratin, type I, 3i; keratin, hair, acidic, 3A

380

		Subclass: type I hair keratin 1; hard keratin, type I, 1; Ha-1; keratin, hair, acidic,1
		Subclass: type I hair keratin 4; hard keratin, type I, 4
		Subclass: type I hair keratin 2; Ha-2; hard keratin, type I, 2; keratin, hair, acidic,2
5		Subclass: keratin 18
		Subclass: cytokeratin 9
	AK009020	
	BAB26030.2	F:2.05 (YtoM) chloride intracellular channel
10		Subclass: chloride intracellular channel 3
		Subclass: Chloride intracellular channel protein 2 (XAP121).
		Subclass: p64 bovine chloride channel-like protein
		Subclass: chloride intracellular channel 1; p64CLCP
		Subclass: Chloride intracellular channel protein 5
15		Subclass: chloride intracellular channel 4
		Subclass: chloride intracellular channel 6; chloride channel form A
		Subclass: H1 chloride channel; p64H1; CLIC4
		Subclass: chloride channel form B
20	NM_025939 NP_080215.1	F:2.05 (7to11) phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase; phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoribosylaminoimidazole succinocarboxamide synthetase
		Alternate: similar to Multifunctional protein ADE2
	J04694	F:2.05 (5to11) collagen
25	AAA50292.1	
		Subclass: alpha 1 type IV collagen preproprotein; collagen IV, alpha-1 polypeptide; collagen of basement membrane, alpha-1 chain
		Subclass: alpha-2 type IV collagen
		Subclass: alpha-3 type IV collagen
		Subclass: alpha 3 type IV collagen, isoform 1, precursor; collagen IV, alpha-3 polypeptide (goodpasture antigen)
30		Subclass: alpha-5 type IV collagen
		Subclass: alpha 5 type IV collagen, isoform 2, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
		Subclass: alpha 5 type IV collagen, isoform 3, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
		Subclass: alpha 5 type IV collagen, isoform 1, precursor; collagen IV, alpha-5 polypeptide; collagen of basement membrane, alpha-5 chain
		Subclass: type IV alpha 6 collagen, isoform A precursor; collagen IV, alpha-6 polypeptide; collagen of basement membrane, alpha-6
35		Alternate: arresten
		Alternate: tumstatin
	U70139	F:2.05 (5to7) nocturnin
	AAB62717.1	
		Alternate: CCR4 carbon catabolite repression 4-like ( <i>S. cerevisiae</i> ); CCR4-like (carbon catabolite repression 4, <i>S. cerevisiae</i> )
40		

NM_008956	F:2.05 (5to19)	
NP_032982.1		polypyrimidine tract binding protein
		Subclass: polypyrimidine tract binding protein, isoform c; RNA binding protein; heterogeneous nuclear ribonucleoprotein polypeptide I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)
		Subclass: polypyrimidine tract binding protein, isoform b; RNA binding protein; heterogeneous nuclear ribonucleoprotein polypeptide I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)
5		Subclass: polypyrimidine tract binding protein, isoform a; RNA binding protein; heterogeneous nuclear ribonucleoprotein polypeptide I; polypyrimidine tract binding protein (heterogeneous nuclear ribonucleoprotein I)
		Subclass: polypyrimidine tract binding protein 2; neural polypyrimidine tract binding protein; PTB-like protein
		Subclass: similar to polypyrimidine-tract binding protein
		Subclass: non-neuronal splice variant nPTB-3
10		Subclass: non-neuronal splice variant nPTB-4
		Subclass: PTB-like protein L
		Subclass: PTB-like protein S
NM_011919	F:2.05 (5to19)	inhibitor of growth family, member 1; inhibitor of growth 1; inhibitor of
NP_036049.1		growth 1 family, member 1
15		Alternate: candidate tumor suppressor p33ING1
		Alternate: p47
		Alternate: p33
		Alternate: p24 is an alternatively spliced transcript of p33/ING1.
20		Alternate: p32 protein
NM_019447	F:2.05 (5to19)	hepatocyte growth factor (HGF) activator
NP_062320.1		
S67386	F:2.05 (5to19)	serum deprivation response protein; serum deprivation response;
25	AAB28953.1	phosphatidylserine-binding protein
		Alternate: leucine-zipper protein FKSG13
NM_008039		
NP_032065.1	F:2.04 (YtoO)	N-formyl peptide receptor
30		Subclass: formyl peptide receptor-like 1; lipoxin A4 receptor (formyl peptide receptor related)
		Subclass: FMLP-related receptor II
		Subclass: formyl peptide receptor-like 2
		Subclass: formyl peptide receptor 1
35		Subclass: fMet-Leu-Phe receptor (fMLP receptor) (N-formyl peptide receptor) (FPR) (N-formylpeptide chemoattractant receptor).
		Subclass: N-formylpeptide receptor fMLP-R-98

	NM_009417		
	NP_033443.1	F:2.04 (YtoM)	Peroxidase
			Subclass: thyroid peroxidase isoform a; thyroperoxidase; thyroid microsomal antigen
			Subclass: thyroid peroxidase isoform b; thyroperoxidase; thyroid microsomal antigen
5			Subclass: thyroid peroxidase isoform c; thyroperoxidase; thyroid microsomal antigen
			Subclass: thyroid peroxidase isoform d; thyroperoxidase; thyroid microsomal antigen
			Subclass: thyroid peroxidase isoform e; thyroperoxidase; thyroid microsomal antigen
			Subclass: thyroid peroxidase isoform 5
10			Subclass: myeloperoxidase
			Subclass: eosinophil peroxidase
			Subclass: lactoperoxidase
	NM_007472	F:2.04 (7to11)	aquaporin (water channel protein)
15	NP_031498.1		Subclass: aquaporin 1 (channel-forming integral protein, 28kD)
			Subclass: major intrinsic protein of lens fiber; aquaporin
			Subclass: aquaporin 2; Aquaporin-2 (collecting duct)
			Subclass: hAQP-CD=collecting duct aquaporin [human, kidney, Peptide, 271 aa]
20			Subclass: aquaporin 4 C2 isoform; mercurial-insensitive water channel
			Subclass: aquaporin 4 isoform a; mercurial-insensitive water channel
			Subclass: aquaporin 4, long splice form - human
			Subclass: aquaporin 5; Aquaporin-5
	NM_029239	F:2.04 (7to11)	
25	NP_083515.1		protein kinase
			Subclass: protein kinase C, nu; serine-threonine protein kinase
			Subclass: Similar to protein kinase C, nu
			Subclass: protein kinase C, mu
			Subclass: protein kinase D2
30			
	AK003830	F:2.04 (7to19)	CGI-128 protein
	BAB23024.1		
	NM_020520	F:2.04 (7to19)	carnitine/acylcarnitine translocase; Carnitine-acylcarnitine translocase;
35	NP_065266.1		carnitine-acylcarnitine carrier; solute carrier family 25 (carnitine/acylcarnitine translocase), member 20
	AK007264	F:2.04 (5to19)	uridine phosphorylase
	BAB24924.1		Alternate: similar to Uridine phosphorylase (UDRPase)
40			
	AK008098	F:2.04 (5to19)	seven transmembrane domain protein
	BAB25453.1		

NM_011017	F:2.04 (5to19)	ornithine transporter
NP 035147.1		Subclass: ornithine transporter 1 (hyperornithinemia-hyperammonemia-homocitrullinuria); ornithine transporter 1
		Subclass: ornithine transporter 2
NM_029796	F:2.04 (5to19)	leucine-rich alpha-2-glycoprotein
NP 084072.1		
NM_021532		
NP 067507.2	F:2.03 (YtoO)	DAPPER1; heptacellular carcinoma novel gene 3
NM_011087		
NP 035217.1	F:2.03 (YtoO)	Immunoglobulin-like receptor
		Subclass: leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1; leukocyte immunoglobulin-like receptor 1; CD85 antigen
		Subclass: immunoglobulin-like receptor 1a
		Subclass: immunoglobulin-like receptor 1c
		Subclass: immunoglobulin-like receptor 1c variant 3
		Subclass: immunoglobulin-like receptor 1c variant 4
		Subclass: leukocyte immunoglobulin-like receptor-2
		Subclass: leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 3; leukocyte immunoglobulin-like receptor 3
		Subclass: leukocyte immunoglobulin-like receptor, subfamily A (without TM domain), member 3; leukocyte immunoglobulin-like receptor 4
		Subclass: leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 5
		Subclass: leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 1; leukocyte immunoglobulin-like receptor 6
		Subclass: leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 2; leukocyte immunoglobulin-like receptor 7
		Subclass: immunoglobulin-like receptor 8
		Subclass: immunoglobulin-like receptor 10 protein
NM_019922	F:2.03	cartilage associated protein
NP 064306.1	(11to19)	Alternate: nucleolar autoantigen (55kD) similar to rat synaptonemal complex
AF385682	F:2.03 (7to11)	EGF-TM7-latrophilin-related protein
AAK62363.1		Alternate: egf-like module containing, mucin-like, hormone receptor-like sequence
		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 1; egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform a

384

		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform b
		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform c
		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform e
		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform d
5		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform g
		Subclass: egf-like module containing, mucin-like, hormone receptor-like sequence 2 isoform f
		Subclass: egf-like module-containing mucin-like receptor 3 isoform a
		Subclass: EGF-like module EMR2
10		Alternate: lectomedin
		Subclass: lectomedin-3
		Subclass: latrophilin 1; KIAA0786 protein; lectomedin-1; latrophilin
		Subclass: lectomedin-1 alpha
		lectomedin-2
15		Subclass: lectomedin-2; KIAA0821 protein
		Alternate: CD97 antigen, isoform 1 precursor; leukocyte antigen CD97; seven-span transmembrane protein
		Alternate: CD97 antigen, isoform 2 precursor; leukocyte antigen CD97; seven-span transmembrane protein
20	NM_008625	F:2.03 (7to19) Mannose receptor C; Subclass: mannose receptor C type 1; mannose
	NP_032651.1	receptor precursor; macrophage mannose receptor
		Subclass: mannose receptor, C type 2; KIAA0709 gene product; endocytic
		receptor (macrophage mannose receptor family); likely ortholog of mouse
		mannose receptor, C type 2
		Alternate: endocytic receptor Endo180
		Alternate: phospholipase A2 receptor 1, 18OkDa; phospholipase A2 receptor
		1, 180kD
25	NM_008991	F:2.03 (7to19)
	NP_033017.1	ATP-binding cassette, sub-family D
		Subclass: ATP-binding cassette, sub-family D, member 3; Peroxisomal
		membrane protein-1 (70kD); peroxisomal membrane protein 1 (70kD,
		Zellweger syndrome); peroxisomal membrane protein-1
		Subclass: ATP-binding cassette, sub-family D (ALD), member 1;
		adrenoleukodystrophy protein
		Subclass: ATP-binding cassette, sub-family D, member 2;
		adrenoleukodystrophy-like 1; hALDR
30	NM_025422	F:2.03 (7to19) KIAA0022 gene product
	NP_079698.1	
	NM_007624	F:2.03 (5to19) chromobox homolog 3; heterochromatin protein HP1 gamma; HP1 gamma

385

	NP_031650.1		homolog; heterochromatin-like protein 1
	NM_013762	F:2.03 (5to19)	
5	NP_038790.1		ribosomal protein
			Subclass: ribosomal protein L3; 60S ribosomal protein L3; HIV-1 TAR
			RNA-binding protein B
			Subclass: similar to ribosomal protein L3; 60S ribosomal protein L3; HIV-1
			TAR RNA-binding protein B
			Alternate: Unknown (protein for IMAGE:3538792)
			Alternate: ARBP-b gene product
10			Alternate: Similar to RIKEN cDNA 1110057H16 gene
	NM_013837	F:2.03 (5to19)	tyrosylprotein sulfotransferase; Subclass: tyrosylprotein sulfotransferase 1
	NP_038865.1		
			Subclass: tyrosylprotein sulfotransferase 2; Tyrosylprotein
			phosphotransferase 2
15			Alternate: hypothetical protein
	NM_016751	F:2.03 (5to19)	similar to Kupffer cell receptor
	NP_058031.1		
			Alternate: unnamed protein product
20			Alternate: Langerhans cell specific c-type lectin; langerin
	NM_008043		
	NP_032069.1	F:2.02 (YtoM)	frequently rearranged in advanced T-cell lymphomas; FRAT1
	NM_008905	F:2.02 (7to19)	hypothetical protein
25	NP_032931.1		
			Alternate: protein tyrosine phosphatase, receptor-type, F interacting protein,
			binding protein 2
			Alternate: similar to hypothetical protein
			Alternate: liprin-beta2
30			Alternate: PTPRF interacting protein, binding protein 1 (liprin beta 1)
			Alternate: KIAA1230 protein
	NM_030693	F:2.02 (7to19)	activating transcription factor 5
	NP_109618.1		
35	NM_008280	F:2.02 (5to19)	
	NP_032306.1		lipase
			Subclass: lipase C precursor
			Subclass: hepatic lipase
40			Subclass: endothelial lipase precursor; endothelial cell-derived lipase
			Subclass: lipoprotein lipase precursor
			Subclass: Similar to lipoprotein lipase
	NM_008407	F:2.02 (5to19)	
45	NP_032433.1		inter-alpha-trypsin inhibitor
			Subclass: pre-alpha (globulin) inhibitor, H3 polypeptide; Inter-alpha
			(globulin) inhibitor, H3 polypeptide; inter-alpha-trypsin inhibitor chain 3

3 86

5

10

15

20

25

		Subclass: Inter-alpha-trypsin inhibitor heavy chain H1 precursor (ITI heavy chain H1) (Inter-alpha-inhibitor heavy chain 1) (Inter-alpha-trypsin inhibitor complex component III) (Serum-derived hyaluronan-associated protein) (SHAP)
		Subclass: inter-alpha-trypsin inhibitor C-terminal
		Subclass: Inter-alpha-trypsin inhibitor heavy chain H2 precursor (ITI heavy chain H2) (Inter-alpha-inhibitor heavy chain 2) (Inter-alpha-trypsin inhibitor complex component IX) (Serum-derived hyaluronan-associated protein) (SHAP)
		Subclass: Inter-alpha-trypsin inhibitor heavy chain H4 precursor (ITI heavy chain H4) (Inter-alpha-inhibitor heavy chain 4) (Inter-alpha-trypsin inhibitor family heavy chain-related protein) (IHRP) (Plasma kallikrein sensitive glycoprotein 120) (PK-120) (GP120) (PRO1851) [Contains: GP57]
	NM_009254 NP_033280.1	F:2.02 (5to19) serine (or cysteine) proteinase inhibitor, clade B (ovalbumin)
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3; squamous cell carcinoma antigen 1
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2; plasminogen activator inhibitor, type II (arginine-serpin)
		Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bomapin)
		Subclass: Similar to serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2
		Subclass: Similar to serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8
		Subclass: leupin
		Subclass: similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)
		Subclass: plasminogen activator inhibitor
		Subclass: hurpin
	NM_009658 NP_033788.1	F:2.02 (5to19) aldo-keto reductase
		Subclass: aldo-keto reductase family 1, member B1; aldehyde reductase 1; aldose reductase; low Km aldose reductase; Lii5-2 CTCL tumor antigen
		Subclass: aldo-keto reductase family 1, member B10; aldose reductase-like 1; aldo-keto reductase family 1, member B11 (aldose reductase-like); aldose



387

30

35

40

45

50

55

		reductase-like peptide; aldose reductase-related protein; small intestine reductase
		Subclass: similar to aldo-keto reductase family 1, member B10 (aldose reductase); aldose reductase-like 1; aldo-keto reductase family 1, member B11 (aldose reductase-like
		Subclass: aldo-keto reductase family 1, member A1; aldehyde reductase; alcohol dehydrogenase
		Subclass: aldo-keto reductase family 1, member D1; steroid-5-beta-reductase, beta polypeptide 1 (3-oxo-5 beta-steroid delta 4-dehydrogenase beta 1); steroid 5-beta-reductase
		Subclass: aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4); chlordecone reductase; type I 3-alpha-HSD; Chlordecone reductase
		Subclass: aldo-keto reductase family 1, member C1; dihydrodiol dehydrogenase 1; dihydrodiol dehydrogenase isoform DD1; type II 3-alpha-hydroxysteroid dehydrogenase; trans-1,2-dihydrobenzene-1,2-diol dehydrogenase; chlordecone reductase homolog; 20 alpha-hydroxysteroid dehydrogenase; aldo-keto reductase C; hepatic dihydrodiol dehydrogenase
		Subclass: similar to aldo-keto reductase
NM_013484 NP_038512.1	F:2.02 (5to19)	complement component
		Subclass: complement component 2 precursor; C3/C5 convertase
		Subclass: complement factor B preproprotein; B-factor, properdin; C3 proactivator; C3 proaccelerator; glycine-rich beta-glycoprotein; C3/C5 convertase
		Subclass: Similar to complement component 2
NM_016969 NP_058665.1	F:2.02 (5to19)	hypothetical protein BC013995
		Alternate: similar to hypothetical protein BC013995
		Alternate: unnamed protein product
NM_019750 NP_062724.1	F:2.02 (5to19)	putative tumor suppressor FUS2
NM_024198 NP_077160.1	F:2.01 (Min)	Peroxidase
		Subclass: glutathione peroxidase 6
NM_010764 NP_033268.1	F:2.01 (7to19)	mannosidase, alpha, class 2B, member 1; mannosidase, alpha B, lysosomal
		Alternate: Similar to mannosidase, alpha, class 2B, member 1; mannosidase, alpha B, lysosomal
NM_019812 NP_062786.1	F:2.01 (7to19)	sirtuin 1; sirtuin (silent mating type information regulation 2, S. cerevisiae, homolog) 1; sirtuin type 1; sir2-like 1; SIR2alpha

388

		Alternate: Unknown (protein for MGC:21066)
5	BC006621 F:2.01 (5to11)	KIAA0907 protein
	AAH06621.1	
		Alternate: Similar to KIAA0907 protein
	AB003502 F:2.01 (5to19)	G1 to S phase transition 1
10	BAA32526.1	
		Alternate: G1 to S phase transition 2
		Alternate: peptide chain release factor 3
		Alternate: similar to peptide chain release factor 3
		Alternate: polypeptide chain release factor 3b
		Alternate: KIAA1038 protein
15		Alternate: unnamed protein product
	AK003237 F:2.01 (5to19)	hypothetical protein IMAGE3455200
	BAB22661.1	
20	NM_008124 F:2.01 (5to19)	
	NP_032150.2	gap junction protein
		Subclass: gap junction protein, beta 1, 32kDa (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked); Gap junction protein, beta-1, 32kD (connexin 32); gap junction protein, beta 1, 32kD (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked)
		Subclass: gap junction protein, beta 2, 26kDa (connexin 26); gap junction protein, beta 2, 26kD (connexin 26)
		Subclass: gap junction protein, beta 6 (connexin 30)
25		Subclass: similar to Gap junction beta-4 protein (Connexin 30.3) (Cx30.3)
		Subclass: gap junction protein, beta 5 (connexin 31.1)
		Subclass: gap junction protein, beta 3, 31kDa (connexin 31); gap junction protein, beta 3, 31kD (connexin 31)
		Subclass: connexin25
		Subclass: similar to Gap junction beta-1 protein (Connexin 32) (Cx32) (GAP junction 28 kDa liver protein)
30		Subclass: gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)
		Subclass: gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)
		Subclass: connexin 43; gap junction protein, alpha 1, 43kD (connexin 43); gap junction protein, alpha 1, 43kD
35	NM_008723 F:2.01 (5to19)	nucleophosmin/nucleoplasmin 3; nucleoplasmin-3;
	NP_032749.1	nucleophosmin/nucleoplasmin family, member 3
	NM_022325 F:2 (7to19)	cathepsin Z; CTSZ
	NP_071720.1	
		Alternate: similar to Cathepsin Z precursor (Cathepsin X) (Cathepsin P)

M62361 AAA40099.1	F:2 (5to19)	sterol carrier protein 2
NM_008331 NP_032357.1	F:2 (5to19)	Unknown (protein for MGC:14710)
		Alternate: <del>interferon</del> -induced protein
		Subclass: <del>interferon</del> -induced protein with tetratricopeptide repeats 1; Interferon, alpha-inducible protein (MW 56kD); interferon-induced protein 56
		Subclass: retinoic acid- and interferon-inducible protein (58kD)
		Subclass: similar to <del>Interferon</del> -induced protein with tetratricopeptide repeats 2 (IFIT-2) ( <del>Interferon</del> -induced 54 kDa protein) (IFI-54K) (ISG-54 K)
		Subclass: <del>interferon</del> -induced protein with tetratricopeptide repeats 4
		Subclass: similar to <del>Interferon</del> -induced protein with tetratricopeptide repeats 4 (IFIT-4) ( <del>Interferon</del> -induced 60 kDa protein) (IFI-60K) (ISG-60) (CIG49) (Retinoic acid-induced gene G protein) (RIG-G)

390

**Subtable 2B: Unfavorable Human Protein Classes**

	Mouse Gene Protein	Behavior	Description
5	NM_007702 NP_031728.1	U:52.77 (YtoO)	cell death activator Subclass: Cell death activator CIDE-A
10	NM_007822 NP_031848.1	U:18.8 (5to7)	cytochrome P450, Subclass: cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega; alkane-1 monooxygenase; lauric acid omega-hydroxylase (CYP4A11) Subclass: cytochrome P450, subfamily IVB, polypeptide 1; cytochrome P450, subfamily IVB, member 1; microsomal monooxygenase Subclass: cytochrome P450, subfamily IVF, polypeptide 2; leukotriene B4 omega-hydroxylase; leukotriene-B4 20-monooxygenase Subclass: cytochrome P450, subfamily IVF, polypeptide 3; leukotriene B4 omega-hydroxylase; leukotriene-B4 20-monooxygenase; cytochrome P450-LTB-omega Subclass: cytochrome P450, subfamily IVF, polypeptide 11
15			Subclass: Cytochrome P450 4F12 (CYP11B2) Subclass: cytochrome P450, subfamily IVF, polypeptide 8; microsomal monooxygenase; flavoprotein-linked monooxygenase Subclass: similar to CYTOCHROME P450 4F6 (CYP11B6) Subclass: cytochrome P-450LTBV
20	NM_008745 NP_032771.1	U:14.81 (YtoO)	Receptor tyrosine kinase Subclass: neurotrophin receptor tyrosine kinase type 2 Subclass: brain-derived neurotrophic factor receptor Subclass: neurotrophin receptor trkC
25			Subclass: TRKA Subclass: High affinity nerve growth factor receptor precursor (TRK1 transforming tyrosine kinase protein) (p 140-TrkA) (Trk-A).
30	NM_026574 NP_080850.1	U:12.76 (3to11)	KIAA1259 protein Alternate: unnamed protein product Alternate: hypothetical protein DKFZp434B0616.1 - human
35	NM_021456 NP_067431.1	U:10.66 (YtoM)	Carboxylesterase Subclass: carboxylesterase 1 (monocyte/macrophage serine esterase 1); liver carboxylesterase; carboxylesterase 2 (liver)

391

		Subclass: brain carboxylesterase hBr1
		Subclass: brain carboxylesterase hBr2
		Subclass: brain carboxylesterase hBr3
		Subclass: acyl coenzyme A:cholesterol acyltransferase
5		Subclass: egasyn
		Subclass: serine esterase N-terminal truncated (503 AA)
		Subclass: carboxylesterase hCE-2
	NM_013641	U:8.87
10	NP_038669.1	(YtoM) prostaglandin E receptor
		Subclass: prostaglandin E receptor, subtype EP1
	AK004768	U:7.6
	BAB23547.1	(YtoO) oxysterol-binding protein-related protein
15		Subclass: oxysterol-binding protein-like protein 3 isoform b; oxysterol-binding protein-related protein 3; ysterol-binding protein 3; OSBP-related protein 3
		Subclass: oxysterol binding protein-related protein 3 isoform 1a
		Subclass: oxysterol binding protein-related protein 3 isoform 1d
		Subclass: oxysterol-binding protein-like protein 3 isoform c; oxysterol-binding protein-related protein 3; oxysterol-binding protein 3; OSBP-related protein 3
		Subclass: oxysterol-binding protein-like protein 3 isoform e; oxysterol-binding protein-related protein 3; oxysterol-binding protein 3; OSBP-related protein 3
20		Subclass: oxysterol-binding protein-like protein 3 isoform f; oxysterol-binding protein-related protein 3; oxysterol-binding protein 3; OSBP-related protein 3
		Subclass: oxysterol binding protein-related protein 3 isoform 2c
		Subclass: oxysterol binding protein-related protein 3 isoform 2d
		Subclass: oxysterol-binding protein-like 1A isoform B; oxysterol-binding protein-related protein 1; oxysterol-binding protein-like 1B; OSBP-related protein 1
		Subclass: oxysterol-binding protein-like 1A isoform C; oxysterol-binding protein-related protein 1; oxysterol-binding protein-like 1B; OSBP-related protein 1
25		Subclass: oxysterol-binding protein-like protein OSBPL1A
		Subclass: Oxysterol-binding protein 2 (Oxysterol binding protein-related protein 4) (OSBP-related protein 4) (ORP-4).
		Subclass: oxysterol-binding protein-like protein 6 isoform b; oxysterol-binding protein-related protein 6; OSBP-related protein 6
		Subclass: OSBP-related protein 7; ORP7
30	AK011986	U:6.54
	BAB27959.1	(7to19) hypothetical protein FLJ32191
		Alternate: zinc finger protein 25
	NM_020568	U:6.5
35	NP_065593.1	(YtoO) KIAA1881 protein

5	NM_013459	U:6.09	
	NP_038487.1	(5to11)	Complement factor D
			Subclass: Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)
			Subclass: Chain , Mutant Of Factor D With Enhanced Catalytic Activity
			Subclass: Chain , Human Complement Factor D In Complex With Isatoic Anhydride Inhibitor
10	NM_008182	U:5.76	glutathione transferase
	NP_032208.1	(5to19)	
			Subclass: glutathione S-transferase A1; GST, class alpha, 1; glutathione S-alkyltransferase A1; glutathione S-aryltransferase A1; S-(hydroxyalkyl)glutathione lyase A1; glutathione S-alkyltransferase A1; GST-epsilon; glutathione S-transferase 2
			Subclass: TPA: glutathione transferase A5
			Subclass: Chain A, Glutathione S-Transferase A1-1 (E.C.2.5.1.18)
15			Subclass: Glutathione S-transferase A3-3 (GST class-alpha)
			Subclass: glutathione S-transferase A3
			Subclass: glutathione S-transferase A2; glutathione S-transferase 2; GST, class alpha, 2; liver GST2; glutathione S-alkyltransferase A2; glutathione S-aryltransferase A2; S-(hydroxyalkyl)glutathione lyase A2; glutathione S-alkyltransferase A2; GST-gamma; HA subunit 2
20	NM_009381	U:5.69	
	NP_033407.1	(YtoO)	Spot14 protein
	AK016553	U:5.55	
	BAB30300.1	(YtoO)	heat shock transcription factor 2 binding protein; heat shock factor 2 binding protein
25	U89406	U:5.43	
	AAC36513.1	(YtoO)	fatty acid synthase
30	NM_025541	U:5.13	
	NP_079817.1	(YtoM)	HSPC146
			Alternate: dJ329L24.2 (hypothetical 23.0 KD protein.)
35	AF281045	U:4.86	ribonuclease L (2',5'-oligoadenylate synthetase-dependent); ribonuclease 4
	AAG33708.1	(5to11)	
			Alternate: A45771
35	AK006096	U:4.75	
	BAB24407.1	(YtoO)	Similar to RIKEN cDNA 1700018O18 gene

	NM_008495	U:4.6	beta-galactosidase binding lectin precursor; Lectin, galactose-binding, soluble, 1;
	NP_032521.1	(7to11)	
5	NM_025429	U:4.44	
	NP_079705.1	(5to19)	serine (or cysteine) proteinase inhibitor
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bomapin)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)
	AF332052	U:4.08	
	AAK56081.1	(YtoO)	ATP citrate lyase
15	AK018226	U:4.01	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin)
	XP_181363.1	(5to19)	
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 10; protease inhibitor 10 (ovalbumin type, bomapin)
			Subclass: serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)
	NM_010831	U:3.91	
	NP_034961.1	(YtoO)	Serine/threonine protein kinase
25			Subclass: SNF1-like kinase
			Subclass: Ser/Thr protein kinase PAR-1A
			Subclass: Ser/Thr protein kinase PAR-1B alpha
			Subclass: MAP/microtubule affinity-regulating kinase like 1; MARK4
			serine/threonine protein kinase
			Subclass: MAP/microtubule affinity-regulating kinase 2 isoform a; ELKL motif kinase 1; ELKL motif kinase

		Subclass: MAP/microtubule affinity-regulating kinase 2 isoform b; ELKL motif kinase 1; ELKL motif kinase
		Subclass: MAP/microtubule affinity-regulating kinase 3 long isoform
		Subclass: Cdc25C associated protein kinase C-TAK1
		Subclass: 5'-AMP-activated protein kinase, catalytic alpha-2 chain (AMPK alpha-2 chain).
5		Subclass: KIAA0781 protein
		Subclass: KIAA0999 protein
	NM_023499 U:3.72	
10	NP_075988.1 (YtoO)	immunoglobulin lambda light chain
		Subclass: immunoglobulin lambda light chain VLJ region
		Subclass: Ig lambda VI THO
		Subclass: Ig lambda chain (BJP-DIA)
		Subclass: Ig lambda, anti-Rh(c).
		Subclass: Ig lambda chain V region
15		
	NM_009255 U:3.6	similar to tropomyosin, fibroblast - human
	NP_033281.1 (5to19)	
		Alternate: Protease Inhibitor; Proteinase Inhibitor
		Subclass: GliA derived nexin precursor (GDN) (Protease nexin I) (PN-1) (Protease inhibitor 7)
20		Subclass: Plasminogen Activator Inhibitor-1; Chain: A; Synonym: Pai-1, Endothelial Plasminogen Activator Inhibitor, Pai
		Subclass: serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1; plasminogen activator inhibitor, type I; Synonym: Pai-1, Endothelial Plasminogen Activator Inhibitor, Pai
		Subclass: pre-beta-migrating plasminogen activator inhibitor
		Subclass: Cleaved Substrate Variant Of Plasminogen Activator Inhibitor-1
		Subclass: Active Form Of Human Pai-1
25		Subclass: serine (or cysteine) proteinase inhibitor, clade I (neuroserpin), member 1; protease inhibitor 12 (neuroserpin)
		Subclass: serine (or cysteine) proteinase inhibitor, clade I (neuroserpin), member 1
		Subclass: protease inhibitor 14; pancpin
	NM_021468 U:3.58	
30	NP_067443.1 (MtoO)	UNC13 (C. elegans)-like; homolog of rat Munc13 (diacylglycerol-binding)
	NM_007643 U:3.57	CD36 antigen (collagen type I receptor, thrombospondin receptor); CD36 antigen
	NP_031669.1 (YtoO)	(collagen type I)
35		
	AK007293 U:3.56	KIAA1879 protein
	BAB24937.1 (5to11)	



	AK008016	U:3.37	
	AK008016	(YtoO)	Similar to RIKEN cDNA 2010001M09 gene
5	NM_013623	U:3.35	orosomucoid 1 precursor; Orosomucoid-1 (alpha-1-acid glycoprotein-1); alpha-1-
	NP_038651.1	(7to19)	acid glycoprotein 1
	NM_020277	U:3.35	transient receptor potential cation channel
	NP_064673.1	(5to11)	
10			Subclass: transient receptor potential cation channel, subfamily M, member 5; MLSN1 and TRP-related; MSLN1- and TRP-related; LTRPC5 protein
			Subclass: transient receptor potential cation channel, subfamily M, member 4
			Subclass: transient receptor potential-related channel 7, a novel putative Ca2+ channel protein
			Subclass: transient receptor potential cation channel, subfamily M, member 2; transient receptor potential-related channel 7, a novel putative Ca2+ channel protein; transient receptor potential channel 7
			Subclass: transient receptor potential cation channel, subfamily M, member 8
15			Subclass: transient receptor potential cation channel, subfamily M, member 6
			Subclass: transient receptor potential cation channel, subfamily M, member 1; melastatin 1
			Subclass: TRP-related cation influx channel
			Subclass: channel-kinase 1
			Subclass: similar to LTRPC7
20			Alternate: melastatin 1
	NM_007809	U:3.27	
	NP_031835.1	(YtoO)	cytochrome P-450
			Subclass: steroid 17alpha-monooxygenase (EC 1.14.99.9) cytochrome P450 17
25			Subclass: aryl hydrocarbon (benzo[a]pyrene) hydroxylase (EC 1.14.14.-) cytochrome P450 1A1
	J00544	U:3.24	immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu
	AAA38673.1	(YtoO)	polypeptides
30	NM_031494	U:3.21	
	NP_113682.1	(YtoM)	Zinc finger protein
	NM_008161	U:3.13	
	NP_032187.2	(YtoO)	glutathione peroxidase
35			Subclass: glutathione peroxidase 3 (EC 1.11.1.9)
			Subclass: extracellular glutathione peroxidase
			Subclass: glutathione peroxidase type 5 (GPX5)

		Subclass: plasma glutathione peroxidase
	NM_025724	U:3.12
5	NP_080000.1	(MtoO) protein for MGC:26598
		Altimate: Protein Similar to RIKEN cDNA 4921510H08 gene product
	NM_011125	U:3.1
	NP_035255.1	(YtoO) phospholipid transfer protein
		Altimate: dJ337O18.1.2 (Phospholipid Transfer Protein (Lipid Transfer Protein II) (isoform 2))
10		Altimate: Similar to phospholipid transfer protein
	NM_012006	U:3.07
	NP_036136.1	(Sto7) Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)
		Altimate: peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein
15		Altimate: Similar to peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein
	NM_008361	U:3.05
	NP_032387.1	(Sto7) interleukin 1, beta; preinterleukin 1 beta; interleukin 1; catabolin
20	NM_013559	U:2.97
	NP_038587.1	(YtoO) heat shock protein
		Subclass: heat shock 105kD; heat shock 105kD alpha; heat shock 105kD beta
		Subclass: heat shock protein 70
		Subclass: similar to HEAT SHOCK 70 KDA PROTEIN 4 (HEAT SHOCK 70-RELATED PROTEIN APG-2) (HSP70RY)
25		Subclass: apg-2
		Subclass: apg-1
		Subclass: heat shock protein (hsp110 family)
		Subclass: HS24/P52
30	AF127033	U:2.97
	AAG02285.1	(YtoO) fatty acid synthase; FAS
	NM_010062	U:2.89
	NP_034192.1	(Sto11) deoxyribonuclease
35		Subclass: deoxyribonuclease II, lysosomal; DNase II, lysosomal
		Subclass: deoxyribonuclease II beta, isoform 1 precursor; DNase II-like a cid
		DNase; endonuclease DLAD

5	NM_011704	U:2.87	
	NP_035834.1	(5to7)	Vanin
			Subclass: Vanin 1 (VNN1); pantetheinase
			Subclass: vanin 3 isoform 1 ; VNN3 protein; pantetheinase
			Subclass: vanin 2, isoform 1 ; Vannin 2; pantetheinase
10			Subclass: vanin 2, isoform 2; Vannin 2; pantetheinase
			Alternate: Biotinidase
	AK018695	U:2.85	
	NP_598527.1	(YtoM)	protein KIAA0143
15			Alternate; KIAA0953 protein
	NM_011674	U:2.84	
	NP_035804.1	(7to19)	Transferase
			Subclass: 2-hydroxyacylsphingosine 1-beta-galactosyltransferase precursor(UDP-galactose-ceramide galactosyltransferase) (Ceramide UDP-galactosyltransferase) (Cerebroside synthase).
20			Subclass: UDP glycosyltransferase 8 (UDP-galactose ceramide galactosyltransferase)
			Subclass: 2-hydroxyacylsphingosine 1-beta-galactosyltransferase (EC 2.4.1.45)
			Subclass: UDP-glucuronosyltransferase 2B17 precursor, microsomal (UDPGT)(C19-steroid specific UDP-glucuronosyltransferase).
			Subclass: UDP-glucuronosyltransferase 2B15
			Subclass: UDP glycosyltransferase 2 family, polypeptide A1; UDP glucuronosyltransferase 2 family, polypeptide A1
25			Subclass: UDP glucuronosyltransferase 1A5
			Subclass: UDP glucuronosyltransferase 1A6
			Subclass: UDP-glucuronosyltransferase 1A7
			Subclass: UDP glucuronosyltransferase 1A8
			Subclass: UDP glycosyltransferase 1 family, polypeptide A9
30			Subclass: UDP-glucuronosyltransferase 1A10
			Subclass: UDP-glucuronosyltransferase 1-2 precursor, microsomal (UDPGT)(UGT-1B) (UGT1*2) (UGT1-02) (UGT1.2) (UGT1A2) (UGT1B) (HLUGP4).
			Subclass: UDP-glucuronosyltransferase 2B
			Subclass: UDP glucuronosyltransferase 2B4
			Subclass: UDP-glucuronosyltransferase 2B7, microsomal (UDPGT)(3,4-catechol estrogen specific) (UDPGTH-2).
35			Subclass: UDP-glucuronosyltransferase (EC 2.4.1.-) 2B-10
	NM_023455	U:2.75	putative N-acetyltransferase Camello 2
	NP_075944.1	(5to19)	
			Alternate: N-acetyltransferase 8; kidney- and liver-specific gene product; kidney- and liver-specific gene

		Alternate: GLA
		Alternate: hypothetical protein TSC501 [imported]
5	NM_023478 NP_075967.1	U:2.74 (5to19)uroplakin 3
	NM_016774 NP_058054.1	U:2.73 (YtoM)ATP synthase
		Subclass: ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide; ATP synthase, H+ transporting, mitochondrial F1 complex, beta
10		
	NM_011146 NP_035276.1	U:2.68 (5to11)peroxisome proliferative activated receptor
		Subclass: peroxisome proliferative activated receptor gamma
		Subclass: peroxisome proliferative activated receptor gamma, isoform 2; PPAR-gamma; peroxisome proliferator activated receptor gamma
15		Subclass: peroxisome proliferative activated receptor gamma, isoform 1; PPAR-gamma; peroxisome proliferator activated receptor gamma
	NM_013771 NP_038799.1	U:2.67 (YtoM)Metalloprotease
		Subclass: ATP-dependent metalloprotease YME1L
20		Subclass: YME1-like 1 isoform 1; ATP-dependent metalloprotease FtsH1 homolog
	AK002979 BAB22492.1	U:2.67 (5to19)calcyon
25	AK005609 BAB24148.1	U:2.62 (5to19)similar to RIKEN cDNA 1700001L19 [Mus musculus]
	X03796 CAA27422.1	U:2.61 (YtoM)Aldolase
30		Subclass: aldolase C
		Subclass: aldolase A
		Subclass: aldolase B
		Subclass: Fructose 1,6-Bisphosphate Aldolase From Human Liver
35	NM_019415 NP_062288.1	U:2.6 (5to11)Solute carrier family 12
		Subclass: Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride cotransporter) (Na-Cl symporter)
		Subclass: solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters),

		Subclass: solute carrier family 12 (potassium/chloride transporters), member 7; potassium/chloride transporter KCC4
		Subclass: solute carrier family 12, (potassium-chloride transporter) member 5
	AK009937	U:2.57
5	BAB26596.1	(YtoM) hypothetical protein FLJ12118
		Alternate: Synthetase
		Subclass: cysteine-tRNA ligase, isoform a; cysteine transase; cysteine-tRNA synthetase
		Subclass: cysteine-tRNA ligase, isoform b; cysteine transase; cysteine-tRNA synthetase
10	NM_023137	U:2.56
	NP_075626.1	(YtoO) ubiquitin-like protein FAT10
	AK015750	U:2.56
15	BAB29956.1	(YtoO) Sulfotransferase
		Subclass: sulfotransferase, estrogen-preferring
		Subclass: thyroid hormone sulfotransferase
		Subclass: sulfotransferase family 1A
		Subclass: sulfotransferase family, cytosolic, 1A, phenol-preferring, member 1
		Subclass: SULT1C sulfotransferase; sulfotransferase family, cytosolic, 1C, member C2
20		Subclass: sulfotransferase 1C1
		Subclass: Phenol-sulfating phenol sulfotransferase 1 (P-PST) (Thermostable phenol sulfotransferase) (Ts-PST) (HAST1/HAST2) (ST1A3).
		Subclass: phenol-preferring phenol sulfotransferase 2
		Subclass: aryl sulfotransferase ST1A2
		Subclass: aryl sulfotransferase ST1A3
25		Subclass: arylamine sulfotransferase
		Subclass: alcohol/hydroxysteroid sulfotransferase; hST a
		Subclass: sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA) - preferring, member 1; sulfotransferase family 2A, dehydroepiandrosterone (DHEA) - preferring, member 1
		Subclass: hydroxysteroid sulfotransferase SULT2B1a
		Subclass: hydroxysteroid sulfotransferase SULT2B1b
30		
	AK002693	U:2.55
	BAB22288.1	(YtoO) diacylglycerol acyltransferase
		Subclass: diacylglycerol O-acyltransferase 2 like 1; iacylglycerolacyltransferase 2-like
		Subclass: diacylglycerol acyltransferase 2
35		
	NM_011214	U:2.54
	NP_035344.1	(MtoO) Protein-tyrosine-phosphatase

400

		Subclass: protein tyrosine phosphatase, receptor type, U isoform 1 precursor; protein tyrosine phosphatase J; protein tyrosine phosphatase receptor omicron
		Subclass: protein tyrosine phosphatase, receptor type, U isoform 2 precursor; protein tyrosine phosphatase J; protein tyrosine phosphatase receptor omicron
		Subclass: protein tyrosine phosphatase, receptor type, U isoform 3 precursor; protein tyrosine phosphatase J; protein tyrosine phosphatase receptor omicron
5		Subclass: protein tyrosine phosphatase receptor omicron
		Subclass: receptor phosphatase PCP-2
		Subclass: FMI protein
		Subclass: protein tyrosine phosphatase, receptor type, K precursor; protein-tyrosine phosphatase, receptor type, kappa; protein-tyrosine phosphatase kappa; protein- tyrosine phosphatase kappa precursor
		Subclass: protein tyrosine phosphatase, receptor type, M precursor; protein tyrosine phosphatase, receptor type, mu polypeptide; protein tyrosine phosphatase mu precursor
10		Subclass: protein tyrosine phosphatase, receptor type, T, isoform 2 precursor; receptor protein tyrosine phosphatase
		Subclass: protein tyrosine phosphatase sigma
		Subclass: protein tyrosine phosphatase, receptor type, sigma, isoform 1 precursor; protein tyrosine phosphatase PTPsigma
		Subclass: protein tyrosine phosphatase, receptor type, sigma, isoform 2 precursor; protein tyrosine phosphatase PTPsigma
		Subclass: protein tyrosine phosphatase, receptor type, sigma, isoform 3 precursor; protein tyrosine phosphatase PTPsigma
		Subclass: protein tyrosine phosphatase, receptor type, sigma, isoform 4 precursor; protein tyrosine phosphatase PTPsigma
15		Subclass: PTPsigma-(brain)
		Subclass: protein tyrosine phosphatase delta
		Subclass: protein tyrosine phosphatase, receptor type, D isoform 4 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta
		Subclass: protein tyrosine phosphatase, receptor type, D isoform 2 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta
		Subclass: protein tyrosine phosphatase, receptor type, D isoform 3 precursor; protein tyrosine phosphatase, receptor type, delta polypeptide; protein tyrosine phosphatase delta
20		Subclass: protein tyrosine phosphatase, receptor type, F, isoform 2 precursor; protein tyrosine phosphatase, receptor type, F polypeptide; receptor-linked protein- tyrosine phosphatase LAR; Leukocyte antigen-related tyrosine phosphatase; LCA- homolog

401

NM_019935 NP_064319.1	U:2.52 (5to11)	OVO-like 1 binding protein; putative transcription factor OVO-like 1; ovo (Drosophila) homolog-like 1
		Alternate: hypothetical protein, similar to (AF134804) putative zinc finger transcription factor OVO1
		Alternate: zinc finger protein 339; ovo-like 2 (Drosophila)
NM_033174 NP_149409.1	U:2.51 (YtoO)	snRNP
		Subclass: snRNP polypeptide B.
NM_008714 NP_032740.1	U:2.5 (5to19)	Neurogenic locus notch homolog protein (Notch)
		Subclass: Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hN1)
		(Translocation-associated notch protein TAN-1)
		Subclass: NOTCH2 protein
		Subclass: Notch3
		Subclass: Notch homolog 4 (Drosophila); Notch, drosophila, homolog of, 4; Notch (Drosophila) homolog 4
		Alternate: transmembrane protein Jagged 1
		Alternate: fibrillin
		Subclass: fibrillin 1; Fibrillin-1
		Subclass: fibrillin 2
		Subclass: similar to fibrillin
NM_019992 NP_064376.1	U:2.47 (YtoO)	BCR downstream signaling 1
NM_019640 NP_062614.1	U:2.47 (YtoM)	Phosphatidylinositol transfer protein
		Subclass: dJ353E16.1 (phosphatidylinositol transfer protein beta)
		Subclass: Phosphatidylinositol transfer protein alpha isoform (PtdIns transfer protein alpha) (PtdInsTP) (PI-TP-alpha).
		Subclass: NIR2
		Subclass: homologue of Drosophila retinal degeneration B gene
		Subclass: PYK2 N-terminal domain-interacting receptor 3; KIAA1457 protein; likely ortholog of mouse retinal degeneration B2 homolog (Drosophila) (Rdgb2)
NM_007824 NP_031850.1	U:2.47 (YtoM)	cytochrome P450
		Subclass: cytochrome P450, subfamily VIIA, polypeptide 1; cholesterol 7-alpha-hydroxylase; cholesterol 7 alpha-monooxygenase
		Subclass: sterol 12-alpha-hydroxylase CYP8B1

		Alternate: prostacyclin synthase
	NM_011076 U:2.45	
5	NP_035206.1 (YtoO)	P glycoprotein. Subclass: ATP-binding cassette, sub-family B (MDR/TAP), member 1; P glycoprotein 1/multiple drug resistance 1; P-glycoprotein-1/multiple drug resistance-1; multidrug resistance 1 Subclass: ATP-binding cassette, subfamily B, member 4 isoform B; P glycoprotein 3/multiple drug resistance 3; P-glycoprotein-3/multiple drug resistance-3; multiple drug resistance 3 Subclass: ATP-binding cassette, subfamily B, member 4 isoform C; P glycoprotein 3/multiple drug resistance 3; P-glycoprotein-3/multiple drug resistance-3; multiple drug resistance 3 Subclass: ATP-binding cassette, sub-family B (MDR/TAP), member 11; ABC member 16, MDR/TAP subfamily; progressive familial intrahepatic cholestasis 2; bile salt export pump
10		Alternate: bile salt export pump
	NM_009345 U:2.43	
	NP_033371.1 (YtoO)	deoxynucleotidyltransferase, terminal; Terminal deoxynucleotidyltransferase Alternate: polymerase (DNA directed), mu; polymerase (DNA-directed), mu
15		
	AK009815 U:2.42	
	BAB26519.1 (YtoO)	1,4-alpha-glucan branching enzyme (EC 2.4.1.18)
	NM_011178 U:2.42	
	NP_035308.1 (YtoM)	Proteinase
20		Subclass: Myeloblastin (Leukocyte proteinase 3) (PR-3) (PR3) (AGP7)(Wegener's autoantigen) (P29) (C-ANCA antigen) (Neutrophil proteinase 4) (NP-4).
		Subclass: proteinase 3
		Subclass: medullasin
		Subclass: Human Heparin Binding Protein
		Subclass: azurocidin
25		Subclass: cationic antimicrobial protein CAP37
		Subclass: leukocyte elastase (EC 3.4.21.37)
	NM_010225 U:2.42	forkhead box F2; forkhead (Drosophila)-like 6
	NP_034355.1 (S to I)	
30		Alternate: transcription factor FREAC-2
		Alternate: forkhead box F1; forkhead (Drosophila)-like 5; Forkhead, drosophila, homolog-like 5; forkhead-related activator 1



5	NM_007760 NP_031786.1	U:2.41 (5to7)	carnitine acetyltransferase
			Subclass: Carnitine O-acetyltransferase (Carnitine acetylase) (CAT)
			Subclass: carnitine acetyltransferase isoform 1
			Subclass: carnitine acetyltransferase isoform 2
			Subclass: carnitine acetyltransferase isoform 3
10	NM_010846 NP_034976.1	U:2.39 (YtoO)	Interferon-induced protein
			Subclass: interferon-induced Mx protein
			Subclass: myxovirus resistance protein 1; interferon inducible protein p78; interferon-regulated resistance GTP-binding protein
			Subclass: interferon-induced viral resistance protein MxB
			Subclass: MX2
15			Alternate: dynamin
			Subclass: dynamin 2; Dynamin II
			Subclass: Dynamin 3 (Dynamin, testicular) (T-dynamin).
20	NM_008151 NP_032177.1	U:2.39 (7to19)	G protein-coupled receptor
			Subclass: G protein-coupled receptor 12
			Subclass: G protein-coupled receptor 3; adenylate cyclase constitutive activator
			Subclass: G protein-coupled receptor 6
25	D00208 BAA00148.1	U:2.39 (5to11)	S100 calcium-binding protein A4; 18A2; 42A; S100 calcium-binding protein A4 (calcium protein, calvasculin, metastasin, murine placental homolog); malignant transformation suppression 1
30	NM_012050 NP_036180.1	U:2.38 (YtoO)	osteomodulin
	NM_019748 NP_062722.1	U:2.38 (YtoM)	SUMO-1 activating enzyme
			Subclass: SUMO-1 activating enzyme subunit 1
35	NM_008273 NP_032299.1	U:2.36 (5to11)	homeo box D11; homeo box 4F; Hox-4.6, mouse, homolog of; homeobox protein Hox-D11
	NM_009676 NP_033806.1	U:2.36 (5to7)	Aldehyde oxidase
			Subclass: aldehyde oxidase 1

		Subclass: Similar to aldehyde oxidase 1
	NM_009773	U:2.35
5	NP_033903.1	(MtoO) mitotic checkpoint protein kinase
		Subclass: MAD3-like protein kinase
		Subclass: budding uninhibited by benzimidazoles 1 Beta
	NM_030127	U:2.32
10	NP_084403.1	(YtoO) serine protease
		Subclass: serine protease HTRA3
		Subclass: protease, serine, 11
		Subclass: serine protease HtrA2-p7
	NM_011086	U:2.32
15	NP_035216.1	(Sto11) unnamed protein product
		Alternate: FYVE finger-containing phosphoinositide kinase (1-phosphatidylinositol-4-phosphate 5-kinase) (PIP5K) (PtdIns(4)P-5-kinase) (p235)
		Alternate: similar to FYVE finger-containing phosphoinositide kinase (1-phosphatidylinositol-4-phosphate kinase) (PIP5K) (PtdIns(4)P-5-kinase) (p235)
		Alternate: hypothetical protein MGC40423
20	V00795	U:2.3
	CAA24176.1	(Sto19) Immunoglobulin heavy chain
		Subclass: immunoglobulin heavy chain constant region
		Subclass: Ig gamma 2 H chain BUR
		Subclass: Ig gamma-2 chain C region
25		Subclass: immunoglobulin gamma 2 heavy chain constant region
		Subclass: recombinant IgG1 heavy chain
		Subclass: immunoglobulin lambda heavy chain
		Subclass: Ig gamma-1 chain C region - human
30	NM_016922	U:2.29
	NP_058618.1	(YtoO) Sulfotransferase
		Subclass: Galactosylceramide sulfotransferase (GalCer sulfotransferase)
		(Cerebroside sulfotransferase) (3'-phosphoadenylylsulfate: galactosylceramide 3'-sulfotransferase) (3'-phosphoadenosine-5'-phosphosulfate: GalCer sulfotransferase)
		Subclass: glycoprotein beta-Gal 3'-sulfotransferase
		Subclass: beta-galactose-3-O-sulfotransferase 3
35		Subclass: beta-galactose-3-O-sulfotransferase, 4
	NM_013739	U:2.29
	NP_038767.1	(YtoM) hypothetical protein FLJ22570

5	NM_008673	U:2.29	
	NP_032699.1	(MtoO)	N-acetyltransferase
			Subclass: arylamine N-acetyltransferase 1
	NM_026189	U:2.29	KIAA1706 protein
10	NP_080465.1	(5to11)	
			Alternate: similar to RIKEN cDNA 2310005P05
			Alternate: unnamed protein product
	AF047725	U:2.28	
15	AAD13720.1	(5to11)	cytochrome P450, subfamily IIC
			Subclass: cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase
			Subclass: cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase
			Subclass: Cytochrome P450 2C8 (CYP11C8) (P450 form 1) (P450 MP-12/MP-20) (P450 IIC2) (S-mephenytoin 4-hydroxylase)
			Subclass: cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase
20			Subclass: Cytochrome P450 2C10 (CYP11C10) (P450 MP-8) (S-mephenytoin 4-hydroxylase) (P-450MP)
	NM_058212	U:2.26	cerebellum D4
	NP_478119.1	(5to19)	
	NM_011897	U:2.25	
25	NP_036027.1	(YtoO)	antagonist of FGF and/or EGF signaling
			Subclass: sprouty (Drosophila) homolog 2
			Subclass: Sprouty homolog 1 (Spry-1).
			Subclass: sprouty homolog 3; antagonist of FGF signaling
30	NM_018861	U:2.25	
	NP_061349.1	(YtoM)	neutral amino acid transporter
			Subclass: solute carrier family 1, member 4; glutamate/neutral amino acid transporter; alanine/serine/cysteine/threonine transporter
			Subclass: solute carrier family 1 (neutral amino acid transporter), member 5
			Subclass: solute carrier family 1 (glial high affinity glutamate transporter), member 3

		Subclass: solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1
		Subclass: solute carrier family 1, member 2; H.sapiens mRNA for glutamate transporter; glutamate/aspartate transporter II; excitatory amino acid transporter 2; glial high affinity glutamate
		Subclass: solute carrier family 1 (glutamate transporter), member 7
		Subclass: neutral amino acid transporter B
5		Subclass: Na <sup>+</sup> -dependent neutral amino acid transporter SATT
		Subclass: sodium-dependent neutral amino acid transporter
		Subclass: Excitatory amino acid transporter 3 (Sodium-dependent glutamate/aspartate transporter 3) (Excitatory amino-acid carrier1) (Neuronal and epithelial glutamate transporter).
		Subclass: neuronal and epithelial glutamate transporter
		Subclass: retinal glutamate transporter EAAT5
10		
	AF126834	U:2.24
	AAD20642.1	(YtoO) Intermediate filament binding protein
		Subclass: Periplakin (195 kDa cornified envelope precursor) (190 kDa paraneoplastic pemphigus antigen).
		Subclass: envoplakin
15		Subclass: Plectin 1 (PLTN) (PCN) (Hemidesmosomal protein 1) (HD1).
		Subclass: bullous pemphigoid antigen 1, isoform 1eA precursor; dystonin; hemidesmosomal plaque protein
		Subclass: bullous pemphigoid antigen 1 isoform 1eB precursor; bullous pemphigoid antigen 1; bullous pemphigoid antigen 1 (230/240kD); dystonin; hemidesmosomal plaque protein
		Subclass: Bullous pemphigoid antigen 1, isoforms 6/9/10 (Trabeculin-beta) (Bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein).
		Subclass: Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein).
20		
	U67189	U:2.23
	AAB50619.1	(YtoM) regulator of G protein signalling 16
	NM_008762	U:2.23
25	NP_032788.1	(5to19) olfactory receptor
		Subclass: olfactory receptor, family 2, subfamily C, member 1
		Subclass: olfactory receptor, family 2, subfamily C, member 3
		Subclass: similar to olfactory receptor, family 2, subfamily C, member 3
		Subclass: Olfactory receptor 2B6 (Hs6M1-32) (Olfactory receptor 6-31) (OR6-31)
30		Subclass: olfactory receptor, family 2, subfamily B, member 2
		Subclass: similar to Olfactory receptor 2B2 (Olfactory receptor 6-1) (OR6-1) (Hs6M1-10)

		Subclass: olfactory receptor, family 2, subfamily H, member 3; Olfactory receptor 2
		Subclass: Olfactory receptor 2H2 (Hs6M1-12)
		Subclass: similar to Olfactory receptor 2H1 (Hs6M1-16) (Olfactory receptor 6-2) (OR6-2) (OLFR42A-9004.14/9026.2)
		Subclass: similar to Olfactory receptor 2J3 (Olfactory receptor 6-6) (OR6-6) (Hs6M1-3)
5		Subclass: similar to Olfactory receptor 2B3 (Olfactory receptor 6-4) (OR6-4) (Hs6M1-1)
		Subclass: olfactory receptor, family 5, subfamily V, member 1
		Subclass: olfactory receptor, family 2, subfamily W, member 1
		Subclass: olfactory receptor, family 2, subfamily J, member
		Subclass: similar to olfactory receptor MOR256-3
10		Subclass: similar to olfactory receptor MOR256-12
		Subclass: similar to olfactory receptor MOR256-14
		Subclass: olfactory receptor 89
		Subclass: similar to olfactory receptor 89
		Subclass: similar to 573K1.15 (nm.17M1-6 (novel 7 transmembrane receptor (rhodopsin family) (olfactory receptor LIKE) protein))
15		Alternate: seven transmembrane helix receptor
		Alternate: similar to seven transmembrane helix receptor
	NM_013746	U:2.22 pleckstrin homology domain containing, family B (evectins) member 1; PH domain
20	NP_038774.1	(YtoO) containing protein in retina 1; PH domain containing, retinal 1
	NM_009613	U:2.22
	NP_033743.1	(MtoO) Metalloprotease/disintegrin-like protein
		Subclass: ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein)
		Subclass: a disintegrin and metalloproteinase domain 22 isoform 2 proprotein; MDC2 delta
25		Subclass: a disintegrin and metalloproteinase domain 22 isoform 3 proprotein; MDC2 delta
		Subclass: a disintegrin and metalloproteinase domain 22 isoform 4 proprotein; MDC2 delta
		Subclass: a disintegrin and metalloproteinase domain 22 isoform 5 proprotein; MDC2 delta
		Subclass: ADAM 22 (A disintegrin and metalloproteinase domain 22) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein 2) (Metalloproteinase-disintegrin ADAM22-3)
30		Subclass: a disintegrin and metalloproteinase domain 8
		Subclass: a disintegrin and metalloproteinase domain 21 preproprotein
		Subclass: a disintegrin and metalloproteinase domain 23
		Subclass: a disintegrin and metalloproteinase domain 28 isoform 1
		Subclass: disintegrin and metalloproteinase domain 19

		Subclass: a disintegrin and metalloproteinase domain 19 isoform 1 preproprotein; meltrin beta
		Subclass: a disintegrin and metalloproteinase domain 19 isoform 2 preproprotein; meltrin beta
		Subclass: a disintegrin and metalloprotease domain 12 isoform 2 preproprotein; A disintegrin and metalloproteinase domain 12 (Meltrin-alpha, mouse, homolog of); meltrin alpha
		Subclass: a disintegrin and metalloproteinase domain 33 isoform alpha; disintegrin and reprotolysin metalloproteinase familyprotein; metalloprotease disintegrin
5		Subclass: a disintegrin and metalloproteinase domain 15 (metargidin)
		Subclass: meltrin-S
		Subclass: metalloprotease-disintegrin meltrin beta
10	NM_008008 NP_032034.1	U:2.22 (5to19) fibroblast growth factor 7 precursor; keratinocyte growth factor
	AF366393 AAK53703.1	U:2.21 (YtoM) Protein phosphatase
		Subclass: protein phosphatase 2 (formerly 2A), regulatory subunit B (PR 52), beta isoform
15		Subclass: protein phosphatase 2A BR gamma subunit
		Subclass: protein phosphatase 2A1 B gamma subunit IMYPNO1
	NM_009127 NP_033153.1	U:2.2 (YtoM) Desaturase
20		Subclass: Acyl-CoA desaturase (Stearoyl-CoA desaturase) (Fatty acid desaturase) (Delta(9)-desaturase).
	NM_016894 NP_058590.1	U:2.2 (5to11) receptor (calcitonin) activity modifying protein 1 precursor; calcitonin receptor-like receptor activity modifying protein 1
25		
	NM_013560 NP_038588.1	U:2.2 (5to7) heat shock protein
		Subclass: heat shock 27kDa protein 1; heat shock 27kD protein 1
		Subclass: heat shock protein 27
		Subclass: Unknown (protein for IMAGE:3906970)
30		Subclass: similar to Heat shock 27 kDa protein (HSP 27) (Stress-responsive protein 27) (SRP27) (Estrogen-regulated 24 kDa protein) (28 kDa heat shock protein
	NM_019977 NP_064361.1	U:2.18 (YtoO) aldehyde reductase (aldose reductase) like 6; similar to mouse aldehyde reductase 6 (renal); myo-inositol oxygenase; kidney-specific protein 32

	NM_031194	U:2.18	
	NP_112471.1	(MtoO)	Organic anion transporter
			Subclass: organic anion transporter 3
			Subclass: solute carrier family 22 member 6 isoform b; renal organic anion transporter 1; para-aminohippurate transporter
5			Subclass: solute carrier family 22 member 6 isoform a; renal organic anion transporter 1; para-aminohippurate transporter
			Subclass: solute carrier family 22 member 6 isoform e; renal organic anion transporter 1; para-aminohippurate transporter
			Subclass: solute carrier family 22 member 7 isoform a; organic anion transporter 2; liver-specific transporter
			Subclass: solute carrier family 22 member 4; organic cation transporter 4; integral membrane transport protein
			Subclass: urate anion exchanger 1 isoform b; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12
10			Subclass: solute carrier family 22 member 1 isoform a; organic cation transporter 1
			Subclass: RST
			Subclass: OAT4
			Subclass: organic anion transporter 2
			Subclass: renal organic anion transporter 1
15			Subclass: hUST3
			Subclass: OCTN1
			Subclass: OCTN2
			Subclass: extraneuronal monoamine transporter
			Subclass: bA288H12.2 (organic cation transporter, liver)
20			Subclass: organic cation transporter OKB1
	NM_020051	U:2.17	putative bHLH transcription factor
	NP_064435.1	(YtoO)	
			Alternate: Achaete-scute homolog 3 (bHLH transcriptional regulator Sgn-1)
25			Alternate: ASCL3
	NM_054048	U:2.16	RE1-silencing transcription factor (REST) co-repressor; co-repressor of Rest; Rest
	NP_473389.1	(YtoO)	co-repressor
30			
	NM_016968	U:2.16	
	NP_058664.1	(YtoO)	Oligodendrocyte transcription factor 1 (Oligo1).
	AF316872	U:2.16	
	AAK28061.1	(YtoM)	PTEN induced putative kinase 1; protein kinase BRPK
35			
	M62766	U:2.16	
	AAA37819.1	(YtoM)	3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase).

	AK006525	U:2.16
	BAB24634.1	(YtoM) Islet cell autoantigen
		Subclass: islet cell autoantigen p69 (diabetes-associated autoantigen p69)
5		Subclass: islet cell autoantigen 1 isoform 1; islet cell autoantigen 1 (69kD); islet cell autoantigen p69
		Subclass: islet cell autoantigen 1 isoform 2; islet cell autoantigen 1 (69kD); islet cell autoantigen p69
	NM_009350	U:2.15
	NP_033376.1	(MtoO) Nuclear RNA-binding protein
10		Subclass: testis nuclear RNA-binding protein
	NM_018779	U:2.15
	NP_061249.1	(5to19) phosphodiesterase
		Subclass: cGMP-inhibited 3',5'-cyclic phosphodiesterase A (Cyclic GMP inhibited phosphodiesterase A) (CGI-PDE A)
15		Subclass: phosphodiesterase 3 A, cGMP-inhibited
		Subclass: cGMP-inhibited cAMP phosphodiesterase (EC 3.1.4.-), myocardial form
		Subclass: cyclic nucleotide phosphodiesterase
		Subclass: phosphodiesterase 3 B, cGMP-inhibited
20	NM_011128	U:2.14
	NP_035258.1	(5to11) pancreatic lipase-related protein
		Subclass: pancreatic lipase-related protein 2
		Subclass: pancreatic lipase-related protein 1
		Alternate: pancreatic lipase
25		
	U36475	U:2.14
	AAC52323.1	(5to11) breast/ovarian cancer susceptibility protein BRCA1
	NM_007836	U:2.14
30	NP_031862.1	(5to19) growth arrest and DNA-damage-inducible, alpha; DNA-damage-inducible transcript 1; DNA damage-inducible transcript-1; DNA damage-inducible transcript 1
	NM_010361	U:2.14
	NP_034491.1	(5to19) glutathione S-transferase
		Subclass: glutathione S-transferase theta 2
35		Subclass: glutathione S-transferase theta 1
		Subclass: similar to Glutathione S-transferase theta 1 (GST class-theta) (Glutathione transferase T1-1)



	NM_008193	U:2.13	
	NP_032219.1	(YtoM)	Guanylate kinase (GMP kinase).
			Subclass: guanylate kinase 1
5	NM_013891	U:2.13	
	NP_038919.1	(MtoO)	prostate epithelium-specific Ets transcription factor
	NM_008542	U:2.13	MAD, mothers against decapentaplegic homolog 6; Mothers against
10	NP_032568.1	(11to19)	decapentaplegic, drosophila, homolog of, 6; MAD (mothers against decapentaplegic, Drosophila) homolog 6
			Alternate: MAD, mothers against decapentaplegic homolog 7; MAD (mothers against decapentaplegic, Drosophila) homolog 7; Mothers against decapentaplegic, drosophila, homolog of, 7
	NM_013607	U:2.13	myosin heavy chain
	NP_038635.1	(5to19)	
15			Subclass: smooth muscle myosin heavy chain
			Subclass: smooth muscle myosin heavy chain 11
			Subclass: smooth muscle myosin heavy chain 11, isoform SM1
			Subclass: smooth muscle myosin heavy chain 11, isoform SM2
			Subclass: smooth muscle myosin heavy chain 11, isoform SM3
20			Subclass: myosin, heavy polypeptide 9, non-muscle
			Subclass: Myosin heavy chain, nonmuscle type B (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMMHC-B)
			Subclass: myosin heavy chain nonmuscle form A
			Subclass: nonmuscle myosin heavy chain (NMHC)
			Subclass: myosin, heavy polypeptide 7, cardiac muscle, beta
25			Subclass: beta-myosin heavy chain
			Subclass: myosin alpha heavy chain, cardiac muscle
			Subclass: similar to cardiac alpha-myosin heavy chain
			Subclass: Myosin heavy chain, fast skeletal muscle, embryonic (Muscle embryonic myosin heavy chain) (SMHCE)
			Subclass: cardiac beta myosin heavy chain
30			Subclass: myosin heavy chain, perinatal skeletal muscle
			Subclass: similar to Myosin heavy chain, skeletal muscle, perinatal (MyHC-perinatal)
			Subclass: myosin, heavy polypeptide 1, skeletal muscle, adult; myosin heavy chain IIX/d
			Subclass: myosin, heavy polypeptide 2, skeletal muscle, adult
			Subclass: myosin, heavy polypeptide 3, skeletal muscle, embryonic
			Subclass: myosin, heavy polypeptide 4, skeletal muscle
35			Subclass: myosin, heavy polypeptide 8, skeletal muscle, perinatal

NM_011067	U:2.12	
NP_035197.1	(YtoM)	Circadian protein homolog
		Subclass: period (Drosophila) homolog 3 hPER3
		Subclass: period 1; period (Drosophila) homolog 1; hPER; Period, drosophila, homolog of; circadian pacemaker protein RIGUI
		Subclass: period 2 isoform 2; period, Drosophila, homolog of, 2; period circadian protein 2
NM_007377	U:2.12	KIAA0641 protein
NP_031403.1	(Sto11)	
		Alternate: KIAA1883 protein
		Alternate: similar to KIAA1883 protein
		Alternate: KIAA1079 protein
NM_008321	U:2.11	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein; Inhibitor of
NP_032347.1	(Sto11)	DNA binding 3, dominant negative, helix-loop-helix
		Alternate: similar to dJ150O5.2 (Inhibitor of DNA binding 3 (dominant negative helix-loop-helix protein, IR21, HEIR-1))
NM_010357	U:2.11	
NP_034487.1	(Sto19)	Glutathione S-transferase
		Subclass: Glutathione S-transferase A3-3 (GST class-alpha)
		Subclass: glutathione S-transferase A3
		Subclass: glutathione S-transferase A1; GST, class alpha, 1; glutathione S-alkyltransferase A1; glutathione S-aryltransferase A1; S-(hydroxyalkyl)glutathione lyase A1; glutathione S-alkyltransferase A1; GST-epsilon; glutathione S-transferase 2
		Subclass: glutathione S-transferase A2; glutathione S-transferase 2; GST, class alpha, 2; liver GST2; glutathione S-alkyltransferase A2; glutathione S-aryltransferase A2; S-(hydroxyalkyl)glutathione lyase A2; glutathione S-alkyltransferase A2; GST-gamma; HA subunit 2
		Subclass: Chain A, Glutathione Transferase A1-1 Complexed With An Ethacrynic Acid Glutathione Conjugate (Mutant R15k)
		Subclass: TPA: glutathione transferase A5
		Subclass: glutathione S-transferase A4; glutathione S-alkyltransferase A4; glutathione S-aryltransferase A4; S-(hydroxyalkyl)glutathione lyase A4; glutathione S-alkyltransferase A4; glutathione transferase A4-4; GST class-alpha; glutathione S-transferase, alpha 4
NM_019393	U:2.1	Polymyositis/scleroderma autoantigen 1 (Autoantigen PM/Sci 1)
NP_062266.1	(YtoM)	(Polymyositis/scleroderma autoantigen 75 kDa) (PM/Sci-75) (P75 polymyositis-scleroderma overlap syndrome associated autoantigen).

5

10

15

20

25

30

NM_009075	U:2.09	
NP_033101.1	(YtoO)	Isomerase
		Subclass: ribose 5-phosphate isomerase A (ribose 5-phosphate epimerase);
		RIBOSE 5-PHOSPHATE ISOMERASE
NM_053082	U:2.09	
NP_444312.1	(YtoM)	Transmembrane protein
		Subclass: Transmembrane 4 superfamily, member 7 (Novel antigen 2) (NAG-2)
		(Tetraspanin 4) (Tspan-4).
		Subclass: tetraspan NET-5
NM_019670	U:2.09	
NP_062644.1	(MtoO)	Diaphanous protein homolog
		Subclass: Diaphanous protein homolog 3 (Diaphanous-related formin 3) (DRF3).
		Subclass: bA218B22.1.1 (novel protein (presumed ortholog of mouse diaphenous-related formin (DIA2)) (isoform 1))
		Subclass: diaphanous 2 isoform 12C
		Subclass: diaphanous 2 isoform 156
		Subclass: Diaphanous protein homolog 2 (Diaphanous-related formin 2) (DRF2).
		Subclass: diaphanous 1; Diaphanous, Drosophila, homolog of, 1; deafness, autosomal dominant 1; diaphanous (Drosophila, homolog) 1; hDia1
		Subclass: bA218B22.1.2 (novel protein (presumed ortholog of mouse diaphenous-related formin (DIA2)) (translation of cDNA DKFZp434C0931 (Em:AL137718)) (isoform 2))
NM_011066	U:2.08	
NP_035196.1	(YtoO)	Circadian protein homolog
		Subclass: period 2 isoform 2; period, Drosophila, homolog of, 2; period circadian protein 2
		Subclass: period 2 isoform 1; PERIOD, DROSOPHILA, HOMOLOG OF, 2; period circadian protein 2
		Subclass: period 1; period (Drosophila) homolog 1; hPER; Period, drosophila, homolog of; circadian pacemaker protein RIGUI
		Subclass: Period circadian protein 3 (hPER3).
		Subclass: KIAA0482 protein
AK017753	U:2.08	
XP_285418	(YtoO)	Zinc finger protein
AB041576	U:2.08	
BAA95060.1	(YtoO)	Hydrolase
		Subclass: nudix (nucleoside diphosphate linked moiety X)-type motif 11;
		hypothetical protein FLJ10628

414

		Subclass: nudix (nucleoside diphosphate linked moiety X)-type motif 4
		Subclass: diphosphoinositol polyphosphate phosphohydrolase type 2 beta
		Subclass: diphosphoinositol polyphosphate phosphohydrolase type 2 alpha
5	S70056	U:2.08
	AAB30620.2	(YtoM) Reductase
		Subclass: crystallin, zeta; quinone oxidoreductase; NADPH:quinone reductase
	L25890	U:2.08
10	AAA72411.1	(YtoM) Receptor protein-tyrosine kinase
		Subclass: ephrin receptor EphB2 isoform 1 precursor; developmentally-regulated eph-related tyrosine kinase; elk-related tyrosine kinase; eph tyrosine kinase 3
		Subclass: Ephrin type-B receptor 2 precursor (Tyrosine-protein kinase receptor EPH-3) (DRT) (Receptor protein-tyrosine kinase HEK5) (ERK)
		Subclass: ephrin receptor EphB2 isoform 2 precursor; developmentally-regulated eph-related tyrosine kinase; elk-related tyrosine kinase; eph tyrosine kinase 3
		Subclass: ephrin receptor EphB1 precursor; eph tyrosine kinase 2; ephrin receptor EphB1
15		Subclass: ephrin receptor EphB3 precursor; human embryo kinase 2; EPH-like tyrosine kinase 2; tyrosine-protein kinase receptor HEK-2
		Subclass: Eph-like receptor tyrosine kinase hEphB1c
		Subclass: EphA4; Hek8; TYRO1 protein tyrosine kinase; ephrin receptor EphA4
		Subclass: EphA7; Hek11; ephrin receptor EphA7
		Subclass: EphA5; Hek7; ephrin receptor EphA5
20		Subclass: EphA3; Ephrin receptor EphA3 (human embryo kinase 1); eph-like tyrosine kinase 1 (human embryo kinase 1); ephrin receptor EphA3
		Subclass: ephrin receptor EphB4 precursor; Ephrin receptor EphB4 (hepatoma transmembrane kinase); Tyro11; ephrin receptor EphB4; hepatoma transmembrane kinase
		Subclass: ephrin receptor EphA8 precursor; ephrin type-A receptor 8 precursor; eph- and elk-related tyrosine kinase; tyrosylprotein kinase; tyrosine-protein kinase receptor eek; protein-tyrosine kinase; hydroxyaryl-protein kinase
		Subclass: ephrin receptor EphB6 precursor; tyrosine-protein kinase-defective receptor; ephrin type-B receptor 6
		EphA2; ephrin receptor EphA2; epithelial cell receptor protein tyrosine kinase
25		EphA1; eph tyrosine kinase 1 erythropoietin-producing hepatoma amplified sequence; oncogene EPH; ephrin receptor EphA1); eph tyrosine kinase 1 (erythropoietin-producing hepatoma amplified sequence); ephrin receptor EphA1
		Subclass: ephrin receptor EPHA3 secreted form
		Subclass: hemopoietic cell kinase
		Subclass: protein-tyrosine kinase hck
		Subclass: viral oncogene yes-1 homolog 1; proto-oncogene tyrosine-protein kinase YES; Yamaguchi sarcoma oncogene; cellular yes-1 protein
30		Subclass: PTK2 protein tyrosine kinase 2 isoform a; focal adhesion kinase 1
		Subclass: PTK2 protein tyrosine kinase 2 isoform b; focal adhesion kinase 1

		Subclass: protein-tyrosine kinase fyn isoform a; proto-oncogene tyrosine-protein kinase fyn; src/yes-related novel gene; src-like kinase; c-syn protooncogene; tyrosine kinase p59fyn(T); OKT3-induced calcium influx regulator
		Subclass: lymphocyte-specific protein tyrosine kinase; oncogene LCK; membrane associated protein tyrosine kinase
		Subclass: v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog; Protooncogene SRC, Rous sarcoma; v-src avian sarcoma(Schmidt-Ruppin A-2) viral oncogene homolog
		Subclass: v-abl Abelson murine leukemia viral oncogene homolog 1 isoform b; Abelson murine leukemia viral (v-abl) oncogene homolog 1
5		Subclass: v-abl Abelson murine leukemia viral oncogene homolog 1 isoform a; Abelson murine leukemia viral (v-abl) oncogene homolog 1
		Subclass: protein-tyrosine kinase fyn isoform b; proto-oncogene tyrosine-protein kinase fyn; src/yes-related novel gene; src-likekinase; c-syn protooncogene; tyrosine kinase p59fyn(T); OKT3-induced calcium influx regulator
		Subclass: protein-tyrosine kinase fyn isoform c; proto-oncogene tyrosine-protein kinase fyn; src/yes-related novel gene; src-likekinase; c-syn protooncogene; tyrosine kinase p59fyn(T); OKT3-induced calcium influx regulator
		Subclass: fer (fps/fes related) tyrosine kinase (phosphoprotein NCP94); fer (fps/fes related) tyrosine kinase
		Subclass: tec protein tyrosine kinase
10		Subclass: protein-tyrosine kinase (EC 2.7.1.112) FAK - human
		Subclass: v-abl Abelson murine leukemia viral oncogene homolog 2 isoform a; Abelson-related protein; arg
		Subclass: v-abl Abelson murine leukemia viral oncogene homolog 2 isoform b; arg; Abelson murine leukemia viral (v-abl) oncogene homolog 2 (arg,
15	NM_023128	U:2.08
	NP_075617.1	(MtoO)
		Plasma membrane protein
		Subclass: Paralectmin
		Subclass: KIAA0270
		Subclass: paralectmin 2
		Subclass: Paln2-AKAP2 fusion protein
20		
	NM_030696	U:2.08
	NP_109621.1	(5to19)
		solute carrier family 16 (monocarboxylic acid transporters)
		Subclass: solute carrier family 16 (monocarboxylic acid transporters), member 1;
		Solute carrier family 16 (monocarboxylic acid transporters),
		Subclass: solute carrier family 16 (monocarboxylic acid transporters), member 3;
		monocarboxylate transporter 3
25		Subclass: solute carrier family 16 (monocarboxylic acid transporters), member 7;
		monocarboxylate transporter 2
		Subclass: monocarboxylate transporter 1

	NM_022888	U:2.08	
	NP_075026.1	(5to19)	folate receptor
			Subclass: folate receptor 1 (adult)
5			Subclass: folate receptor 3
			Subclass: folate binding protein
	NM_019811	U:2.07	
	NP_062785.1	(YtoM)	Acetyl-CoA synthetase
			Subclass: acetyl-CoA synthetase isoform a; cytoplasmic acetyl-coenzyme A synthetase; acetate-CoA ligase; acyl-activating enzyme; acetate thiokinase; <del>acetyl-CoA synthetase</del>
10			Subclass: acetyl-CoA synthetase isoform b; cytoplasmic acetyl-coenzyme A synthetase; acetate-CoA ligase; acyl-activating enzyme; acetate thiokinase; <del>acetyl-CoA synthetase</del>
			Subclass: dJ568C11.3 (novel AMP-binding enzyme similar to acetyl-coenzyme A synthetase (acetate-coA ligase))
			Subclass: KIAA1846 protein
			Subclass: dJ18C9.1.3 (similar to acetyl-coenzyme A synthetase, isoform 3)
15	NM_016675	U:2.06	
	NP_057884.1	(YtoM)	Claudin
			Subclass: claudin 2
	NM_011414	U:2.05	
20	NP_035544.1	(YtoO)	Protease inhibitor
			Subclass: secretory leukocyte protease inhibitor; antileukoproteinase; seminal proteinase inhibitor; mucus proteinase inhibitor
	U89924	U:2.05	protein phosphatase 1, regulatory (inhibitor) subunit 5; Phosphatase 1, regulatory
25	AAB49689.1	(5to7)	inhibitor subunit 5
	NM_016878	U:2.04	
	NP_058574.1	(YtoM)	Aminopeptidase
			Subclass: aspartyl aminopeptidase
30	NM_010421	U:2.04	
	NP_034551.1	(YtoM)	Aminidase
			Subclass: hexosaminidase A preproprotein; beta-hexosaminidase alpha chain; beta-N-acetylhexosaminidase; N-acetyl-beta-glucosaminidase
			Subclass: N-acetyl-alpha-glucosaminidase
			Subclass: N-acetyl-beta-glucosaminidase
35			Subclass: hexosaminidase B preproprotein; beta-hexosaminidase beta chain; beta-N-

417

		acetylhexosaminidase; N-acetyl-beta-glucosaminidase
	NM_019430	U:2.04
	NP_062303.1	(YtoM)
		Voltage-dependent calcium channel
		Subclass: voltage-dependent calcium channel gamma-3 subunit; neuronal voltage-gated calcium channel gamma-3 subunit
40		Subclass: voltage-dependent calcium channel gamma-2 subunit; stargazin; neuronal voltage-gated calcium channel gamma-2 subunit
		Subclass: voltage-dependent calcium channel gamma-4 subunit; neuronal voltage-gated calcium channel gamma-4 subunit
		Subclass: voltage-dependent calcium channel gamma-8 subunit; neuronal voltage-gated calcium channel gamma-8 subunit
	NM_010444	U:2.04
45	NP_034574.1	(MtoO)
		Nuclear receptor
		Subclass: nuclear receptor subfamily 4, group A, member 1 isoform a; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3 orphan receptor; steroid receptor TR3
		Subclass: TR3 orphan receptor
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform a; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform d; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
50		Subclass: NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform b; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: Nuclear hormone receptor NOR-1 (Neuron-derived orphan receptor 1) (Mitogen induced nuclear orphan receptor)
		Subclass: nuclear receptor subfamily 4, group A, member 3 isoform b; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor
		Subclass: steroid/thyroid orphan receptor homolog gene
		Subclass: nuclear receptor subfamily 4, group A, member 3 isoform a; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor
55		

			Subclass: mitogen induced nuclear orphan receptor
			Subclass: nuclear receptor subfamily 4, group A, member 1 isoform b; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3 orphan receptor; steroid receptor TR3
			Subclass: nuclear receptor subfamily 4, group A, member 2 isoform c; xmr related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/mur77 beta-type transcription factor homolog
5	NM_023740 NP_076229.1	U:2.04 (5to11)	PP3774
			Alternate: Similar to RIKEN cDNA 1500015N03 gene
			Alternate: similar to Abl-philin 2
			Alternate: Abl-philin 2
10	NM_030566 NP_085043.1	U:2.04 (5to11)	Fos-related antigen
	AK004631	U:2.04	Phosphomannomutase
15	BAB23425.1	(5to19)	
			Subclass: Phosphomannomutase 1 (PMM 1) (PMMH-22)
			Subclass: phosphomannomutase 2
	NM_011498	U:2.03	
20	NP_035628.1	(YtoM)	Basic helix-loop-helix domain containing transcription factor
			Subclass: differentiated embryo chondrocyte expressed gene 1
			Subclass: bHLH transcription factor DEC1
			Subclass: basic helix-loop-helix domain containing, class B, 3; bHLH protein DEC2
25	NM_025703	U:2.03	
	NP_079979.1	(YtoM)	hypothetical protein MGC45400
	AK012163	U:2.03	unnamed protein product
	BAB28070.1	(7to11)	
30			Alternate: hypothetical protein FLJ10998
	NM_010368	U:2.02	
	NP_034498.1	(YtoM)	glucuronidase
			Subclass: glucuronidase, beta
35			



	NM_009998	U:2.02	cytochrome P450, subfamily IIB (phenobarbital-inducible), polypeptide 6
	NP_034128.1	(11to19)	
5	NM_019692	U:2.02	Ras-like without CAAX 2; Ric-like, expressed in neurons (Drosophila); GTP-binding protein Roc2
	NP_062666.1	(5to19)	
			Alternate: Ras family small GTP binding protein RIN
			Alternate: RIBA
10			Alternate: Ras-like without CAAX 1; Ric-like, expressed in many tissues (Drosophila); GTP-binding protein Roc1
	NM_025721	U:2.02	glycosylated 38 kDa sperm protein C-7/8 precursor
	NP_079997.1	(5to19)	
15	NM_009708	U:2.01	
	NP_033838.1	(YtoO)	GTP-binding protein
			Subclass: GTP-binding protein Rho7
			Subclass: ras homolog gene family, member E; Rho8; RhoE
20			Subclass: GTP-binding protein RHO6
	NM_012042	U:2.01	
	NP_036172.1	(YtoM)	Cullin proteins
			Subclass: cullin 1
25			Subclass: cullin 2
			Subclass: cullin 3
			Subclass: Vasopressin-activated calcium-mobilizing receptor (VACM-1) (Cullin homolog 5) (CUL-5)
			Subclass: cullin 4B; Cullin-4B
30			Subclass: cullin 4A
	AK010827	U:2.01	
	BAB27209.1	(YtoM)	hypothetical protein FLJ12660
35	NM_010107	U:2.01	ephrin A1; eph-related receptor tyrosine kinase ligand 1 (tumour necrosis factor, alpha-induced protein 4)
	NP_034237.1	(5to7)	
35	NM_011710	U:2	
	NP_035840.1	(YtoM)	tRNA synthetase
			Subclass: Tryptophanyl-tRNA synthetase (Tryptophan--tRNA ligase) (TRPRS); interferon-induced protein 53 (IFP53) (hWRS).

NO TEXT

**Subtable 2C: Mixed Human Protein Classes**

Mouse Gene Protein	Behavior	Description
AK004731	F:-2.07 (YtoM)	
5 XP_148015	U:+2.71 (7to19)	plakophilin
		Subclass: plakophilin 2
		Subclass: plakophilin 2a
NM_009922	F:-2.54 (YtoO)	
10 NP_034052.1	U:+2.55 (7to19)	calponin
		Subclass: calponin 1, basic, smooth muscle; calponins, basic; Calponin 1
		Subclass: calponin 2; Calponin 2
		Subclass: calponin 3; calponin, acidic
15 NM_021291	F:-2.11 (YtoM)	
NP_067266.1	U:+3.03 (5to19)	amino acid transporter
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 9; solute carrier family 7, member 9; solute carrier family 7 (cationic amino acid, transporter, y+ system), member 9
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 5; Membrane protein E16; Solute carrier family 7, member 5; 4F2 light chain
		Subclass: solute carrier family 7, (cationic amino acid transporter, y+ system) member 11; cystine/glutamate transporter
20		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 7
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 6
		Subclass: solute carrier family 7 (cationic amino acid transporter, y+ system), member 8
		Subclass: Y+L amino acid transporter 1 (y(+)-L-type amino acid transporter 1) (y+LAT-1) (Y+LAT1) (Monocyte amino acid permease 2) (MOP-2).
		Subclass: solute carrier family 7, member 10; a.s.c.-type amino acid transporter 1
		Subclass: Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2).
25		
NM_033373	F:-2.05 (YtoO)	
NP_203537.1	U:+2.12 (7to19)	keratin

		Subclass: keratin 23 isoform a; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cytokeratin 23; type I intermediate filament cytokeratin; histone deacetylase inducible keratin 23, (Cytokeratin 23) (K23) (CK 23).
		Subclass: keratin 23 isoform b; hyperacetylation-inducible type I keratin; keratin, type I cytoskeletal 23; cytokeratin 23; type I intermediate filament cytokeratin; histone deacetylase inducible keratin 23
		Subclass: keratin 20, type I-like, cytoskeletal
		Subclass: keratin 19; keratin, type I cytoskeletal 19; keratin, type I, 40-kd; cytokeratin 19; (Cytokeratin 19) (K19) (CK 19).
5		Subclass: keratin 17
		Subclass: keratin 12 (Meesmann corneal dystrophy); Keratin-12; keratin 12
		Subclass: keratin 15; keratin-15, basic; keratin-15, beta; type I cytoskeletal 15; cytokeratin 15; (Cytokeratin 15) (K15) (CK 15).
		Subclass: keratin 13; keratin, type I cytoskeletal 13; cytokeratin 13
10		Subclass: keratin 16; keratin, type I cytoskeletal 16; cytokeratin 16
		Subclass: keratin 14; cytokeratin 14
		Subclass: type I hair keratin 6; keratin, hair, acidic, 6
		Subclass: cytokeratin 20
		Subclass: type I hair keratin 5; Ha-5; hard keratin, type I, 5
		Subclass: Keratin, type I cytoskeletal 10 (Cytokeratin 10) (K10) (CK 10).
15		Subclass: type I hair keratin 3A; Ha-3I; hard keratin, type I, 3I; keratin, hair, acidic, 3A
		Subclass: type I hair keratin 1; hard keratin, type I, 1; Ha-1; keratin, hair, acidic, 1
		Subclass: type I hair keratin 4; hard keratin, type I, 4
		Subclass: type I hair keratin 2; Ha-2; hard keratin, type I, 2; keratin, hair, acidic, 2
		Subclass: keratin 18
20		Subclass: cytokeratin 9
	X93035 F:-2.87 (YtoO)	
	CAA63603.1 U:-2.78 (Sto19)	chitinase
		Subclass: chitinase 3-like 1; cartilage glycoprotein-39
25		Subclass: chitinotrioidase; plasma methylumbelliferyl tetra-N-acetylchitinotetraoside hydrolase
		Subclass: chitinase 3-like 2; chondrocyte protein 39
		Alternate: oviductal glycoprotein
		Subclass: oviductal glycoprotein 1, 120kDa (mucin 9, oviductin); mucin 9 (oviductin); oviductal glycoprotein 1, 120kDa (mucin 9, oviductin)

NM_010444	U:2.04 (MtoO)	
NP_034574.1	F:-2.6 (7to11)	Nuclear receptor
		Subclass: nuclear receptor subfamily 4, group A, member 1 isoform a; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3 orphan receptor; steroid receptor TR3
		Subclass: TR3 orphan receptor
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform a; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform d; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform b; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
		Subclass: Nuclear hormone receptor NOR-1 (Neuron-derived orphan receptor 1) (Mitogen induced nuclear orphan receptor)
		Subclass: nuclear receptor subfamily 4, group A, member 3 isoform b; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor
		Subclass: steroid/thyroid orphan receptor homolog gene
		Subclass: nuclear receptor subfamily 4, group A, member 3 isoform a; chondrosarcoma, extraskeletal myxoid, fused to EWS; translocated in extraskeletal chondrosarcoma; neuron derived orphan receptor; mitogen induced nuclear orphan receptor
		Subclass: mitogen induced nuclear orphan receptor
		Subclass: nuclear receptor subfamily 4, group A, member 1 isoform b; hormone receptor; growth factor-inducible nuclear protein N10; early response protein NAK1; orphan nuclear receptor HMR; TR3 orphan receptor; steroid receptor TR3

		Subclass: nuclear receptor subfamily 4, group A, member 2 isoform c; nur related protein-1 (mouse), human homolog of; transcriptionally inducible nuclear receptor related 1; intermediate-early receptor protein; T-cell nuclear receptor NOT; orphan nuclear receptor NURR1; NGFI-B/nur77 beta-type transcription factor homolog
	NM_010831	U:3.91 (YtoO)
5	NP_034961.1	F:-2.39 (11to19) Serine/threonine protein kinase
		Subclass: SNF1-like kinase
		Subclass: Ser/Thr protein kinase PAR-1A
		Subclass: Ser/Thr protein kinase PAR-1B alpha
		Subclass: MAP/microtubule affinity-regulating kinase like 1; MARK4 serine/threonine protein kinase
		Subclass: MAP/microtubule affinity-regulating kinase 2 isoform a; ELKL motif kinase 1; ELKL motif kinase
10		Subclass: MAP/microtubule affinity-regulating kinase 2 isoform b; ELKL motif kinase 1; ELKL motif kinase
		Subclass: MAP/microtubule affinity-regulating kinase 3 long isoform
		Subclass: Cdc25C associated protein kinase C-TAK1
		Subclass: 5'-AMP-activated protein kinase, catalytic alpha-2 chain (AMPK alpha-2 chain).
		Subclass: KIAA0781 protein
15		Subclass: KIAA0999 protein
	NM_010846	U:2.39 (YtoO)
	NP_034976.1	F:-2.2 (5to7) Interferon-induced protein
		Subclass: interferon-induced Mx protein
20		Subclass: myxovirus resistance protein 1; interferon inducible protein p78; interferon-regulated resistance GTP-binding protein
		Subclass: interferon-induced viral resistance protein MxB
		Subclass: MX2
		Alternate: dynamin
		Subclass: dynamin 2; Dynamin II
25		Subclass: Dynamin 3 (Dynamin, testicular) (T-dynamin).
	NM_025703	U:2.03 (YtoM)
	NP_079979.1	F:-2.7 (5to19) hypothetical protein MGC45400
30	NM_033174	U:2.51 (YtoO)
	NP_149409.1	F:-2.07 (5to11) snRNP
		Subclass: snRNP polypeptide B.

425

U67189	U:2.23 (YtoM)	
AAB5O619.1	F:-3.57 (5to11)	regulator of G protein signalling 16

**Master Tables 101-199**

In the related applications set forth at the beginning of the specification, we have looked at differential expression of genes in various organs and tissue with respect to (1) aging, (2) hyperinsulinemia and/or type II diabetes. Master Tables 101-199 (note that some of these table numbers are reserved for future use) tabulate those mouse genes which appear both in Master Table 1 of this application, and in the corresponding table of at least one of the related applications.

The following human proteins are considered to be of particular interest:

Human proteins corresponding to mouse genes listed as favorable both in Master Table 1 and in at least one of Master Tables 101-199, which are not listed as unfavorable in any of Master Tables 101-199; and

Human proteins corresponding to mouse genes listed as unfavorable both in Master Table 1 and in at least one of Master Tables 101-199, which are not listed as favorable in any of Master Tables 101-199.



Master Table 101			
Genes Differentially Expressed With Respect to Age in Both Liver and Muscle			
Mouse Gene	Mouse Description	Liver Aging Behavior	Muscle Aging Behavior
AF281045	Mus musculus 2-5A-dependent RNase L mRNA, complete cds	U:4.86 (Sto11)	U:+2.12
AF316872	Mus musculus protein kinase BRPK mRNA, complete cds	U:2.16 (YtoM)	U:+2.26 F:3.65
AK015750	AK015750 Mus musculus adult male testis cDNA, RIKEN full-length enriched library, clone:4930511F10:sulfotransferase, estrogen preferring, full insert sequence	U:2.56 (YtoO)	U:+7.39
AK018226	Mus musculus adult male medulla oblongata cDNA, RIKEN full-length enriched library, clone:6330533H24, full insert sequence	U:4.01 (Sto19)	F:2.35
J04694	MUSCOL1A4A Mus musculus alpha-1 type IV collagen (Col4a-1) mRNA, complete cds	F:2.05 (Sto11)	F:6.66
NM_007702	Mus musculus cell death-inducing DNA fragmentation factor, alpha subunit-like effector A (Cidea), mRNA	U:52.77 (YtoO)	U:+1.88
NM_007952	Mus musculus glucose regulated protein, 58 kDa (Grp58), mRNA	F:2.65 (Sto19)	F:2.59
NM_008161	Mus musculus glutathione peroxidase 3 (Gpx3), mRNA	U:3.13 (YtoO)	U:+2.43
NM_008524	Mus musculus lumican (Lum), mRNA	F:2.41 (Sto19)	F:2.01
NM_009075	Mus musculus ribose 5-phosphate isomerase A (Rpia), mRNA	U:2.09 (YtoO)	F:2.48
NM_009242	Mus musculus secreted acidic cysteine rich glycoprotein (Sparc), mRNA	F:2.73 (Sto19)	F:4.66
NM_009381	Mus musculus thyroid hormone responsive SPOT14 homolog (Rattus) (Thrsp), mRNA	U:5.69 (YtoO)	F:2.18
NM_010238	Mus musculus bromodomain-containing 2 (Brd2), mRNA	F:2.33 (Yto19)	F:2.27
NM_010917	Mus musculus nidogen 1 (Nid1), mRNA	F:2.3 (Sto11)	F:2.54
NM_011579	Mus musculus T-cell specific GTPase (Tgtp), mRNA	F:2.1 (Sto19)	U:+2.72
NM_016906	Mus musculus SEC61, alpha subunit (S. cerevisiae) (Sec61a), mRNA	F:2.37 (Sto19)	U:+2.79 F:3.89
NM_019750	Mus musculus N-acetyltransferase 6 (Nat6), mRNA	F:2.02 (Sto19)	F:2.55
NM_019824	Mus musculus actin related protein 2/3 complex, subunit 3 (21 kDa) (Arpc3), mRNA	F:5.75 (Yto19)	U:+2.14
NM_021301	Mus musculus solute carrier family 15 (H+/peptide transporter), member 2 (Slc15a2), mRNA	F:3.08 (YtoM)	F:2.35
NM_022434	Mus musculus cytochrome P450, subfamily IVF, polypeptide 14 (leukotriene B4 omega hydroxylase) (Cyp4f14), mRNA	F:2.19 (Sto19)	U:+2.12
NM_023184	Mus musculus Kruppel-like factor 15 (Klf15), mRNA	F:2.87 (Sto11)	U:+2.85 F:4.85

428

NM_026189	Mus musculus RIKEN cDNA 2310005P05 gene (2310005P05Rik), mRNA	U:2.29 (Sto11)	U:+2.14
NM_026346	Mus musculus RIKEN cDNA 4833442G10 gene (4833442G10Rik), mRNA	F:3.64 (YtoO)	U:+6.12
U89415	MMU89415 Mus musculus strain BALB/c elongation factor 2 mRNA, partial cds	F:2.73 (Sto19)	U:+2.02 F:2.92

5

Table 102: Mouse Genes Differentially Expressed in Liver with respect to both Diabetes/Hyperinsulinemia and Aging

Gene	Description	Behavior Diabetes	Behavior Aging
AF047725	Mus musculus CYP2C38 (Cyp2c38) mRNA, partial cds	F: (IR-D) 2.06 U: (C-D) 2.35	U: 2.28 (5to11)
AF127033	Mus musculus fatty acid synthase mRNA, complete cds	F: (IR-D) 2.1	U: 2.97 (YtoO)
AF294617	Mus musculus inducible 6-phosphofructo-2-kinase mRNA, complete cds	F: (C-IR) 2.63	F2.69 (5to7)
AF385682	Mus musculus ETL1 mRNA, complete cds	F: (C-IR) 2.04, U: (IR-D) 2.02	F2.03 (7to11)
AK002693	Mus musculus adult male kidney cDNA, RIKEN full-length enriched library, clone:0610030A14:related to COSMID W01A11, full insert sequence	U: (C-IR) 2.04	U: 2.55 (YtoO)
AK002979	Mus musculus adult male brain cDNA, RIKEN full-length enriched library, clone:0710001P07:homolog to D1 DOPAMINE RECEPTOR INTERACTING PROTEIN CALCYON, full insert sequence	F: (C-IR) 2.14, F: (C-D) 2.15	U: 2.67 (5to19)
AK002979	Mus musculus adult male brain cDNA, RIKEN full-length enriched library, clone:0710001P07:homolog to D1 DOPAMINE RECEPTOR INTERACTING PROTEIN CALCYON, full insert sequence	F: (C-IR) 2.14, F: (C-D) 2.15	U: 2.67 (5to19)
AK005274	Mus musculus adult male cerebellum cDNA, RIKEN full-length enriched library, clone:1500017E18:homolog to HYDROXYACYLGLUTATHIONE HYDROLASE (EC 3.1.2.6) (GLYOXALASE II) (GLX II), full insert sequence	U: (C-IR) 2.22, U: (C-D) 2.15	F3.89 (5to7)
AK005535	Mus musculus adult female placenta cDNA, RIKEN full-length enriched library, clone:1600025H15:homolog to CDNA FLJ20327 FTS, CLONE HEP10012, full insert sequence	F: (C-IR) 2.06, F: (C-D) 2.16	F3.25 (YtoM)
AK006096	AK006096 Mus musculus adult male testis cDNA, RIKEN full-length enriched library, clone:1700018018:hypothetical protein, full insert sequence	U: (C-IR) 2.24	U: 4.75 (YtoO)
AK007264	Mus musculus adult male testis cDNA, RIKEN full-length enriched library, clone:1700124F02:homolog to WUGSC:H NH0335J18.1 PROTEIN, full insert sequence	F: (C-IR) 2.95, U: (IR-D) 2.34	F2.04 (5to19)
AK007293	Mus musculus adult male testis cDNA, RIKEN full-length enriched library, clone:1700126L06:unclassifiable, full insert sequence	U: (C-D) 2.19, U: (IR-D) 2.62	U: 3.56 (5to11)
AK009563	Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310032D16, full insert sequence	F: (C-IR) 2.33	F2.1 (5to19)

5	AK018226	Mus musculus adult male medulla oblongata cDNA, RIKEN full-length enriched library, clone:6330533H24, full insert sequence	F: (C-IR) 2.53, F: (C-D) 2.4	U: 4.01 (Sto19)
	M12571	MUSHSP68A Mouse heat shock protein (hsp68) mRNA, clone MHS243, partial cds	U: (C-IR) 3.58	F2.73 (YtoM)
	M12573	MUSHSP68C Mouse heat shock protein (hsp68) mRNA, clone MHS214, partial cds	U: (C-D) 2.94	F2.07 (Sto19)
	M62766	MUSHMGCOA Mouse HMG-CoA reductase mRNA, 3' end	U: (C-IR) 2.02	U: 2.16 (YtoM)
	M63245	MUSALASH Mus musculus amino levulinate synthase (ALAS-H) mRNA, 3' end	U: (C-IR) 3.05	F3.98 (Sto19)
	NM_007468	Mus musculus apolipoprotein A-IV (Apoa4), mRNA	U (C-IR) 2.98, U (C-D) 2.42, U (IR-D) 2.16	F2.22 (7to11)
	NM_007472	Mus musculus aquaporin 1 (Aqp1), mRNA	F: (C-IR) 2.17, U: (IR-D) 2.38	F2.04 (7to11)
	NM_007489	Mus musculus aryl hydrocarbon receptor nuclear translocator-like (Arnt1), mRNA	F: (C-D) 2.13	F2.22 (7to11)
	NM_007643	Mus musculus CD36 antigen (Cd36), mRNA	F: (C-IR) 3.03, U: (C-D) 2.05, U: (IR-D) 3.33	U: 3.57 (YtoO)
	NM_007702	Mus musculus cell death-inducing DNA fragmentation factor, alpha subunit-like effector A (Cidea), mRNA	U: (C-D)+ 4.7	U: 52.77 (YtoO)
10	NM_007706	Mus musculus cytokine inducible SH2-containing protein 2 (Cish2), mRNA	F: (C-D) 2.51	F4.4 (YtoM)
	NM_007760	Mus musculus carnitine acetyltransferase (Crat), mRNA	U: (C-IR) 2.57, U: (C-D) 2.16	U: 2.41 (Sto7)
	NM_007809	Mus musculus cytochrome P450, 17 (Cyp17), mRNA	U: (C-IR) 3.41, U: (C-D) 3.69	U: 3.27 (YtoO)
	NM_007811	Mus musculus cytochrome P450, 26, retinoic acid (Cyp26), mRNA	F: (C-IR) 17.03, F: (C-D) 3.81	F2.08 (Sto11)
	NM_007822	Mus musculus cytochrome P450, 4a14 (Cyp4a14), mRNA	U: (C-IR) 24.5, F: (C-D) 5.06, F: (IR-D) 7.06	U: 18.8 (Sto7)
15	NM_007824	Mus musculus cytochrome P450, 7a1 (Cyp7a1), mRNA	F: (C-IR) 2.14, F: (C-D) 3.09	U: 2.47 (YtoM)

NM_007825	Mus musculus cytochrome P450, 7b1 (Cyp7b1), mRNA	F: (C-IR) 6.41, U: (IR-D) 5.83	F2.22 (5to19)
NM_007860	Mus musculus deiodinase, iodothyronine, type I (Dio1), mRNA	U: (C-IR) 2.84, U: (C-D) 2.06	F2.06 (7to19)
NM_007912	Mus musculus epidermal growth factor receptor (Egfr), mRNA	F: (C-IR) 2.09, F: (C-D) 2.69	F2.21 (5to19)
NM_008039	Mus musculus formyl peptide receptor, related sequence 2 (Fpr-rs2), mRNA	F: (C-D)- 2.4	F2.04 (Yto0)
NM_008061	Mus musculus glucose-6-phosphatase, catalytic (G6pc), mRNA	F: (C-IR) 2.28, F: (C-D) 2.14	F2.75 (5to11)
NM_008182	Mus musculus glutathione S-transferase, alpha 2 (Yc2) (Gsta2), mRNA	F: (C-IR) 9.17, F: (C-D) 5.68	U: 5.76 (5to19)
NM_008245	Mus musculus hematopoietically expressed homeobox (Hhex), mRNA	F: (C-D) 2.62, U: (IR-D) 2.05	F2.2 (7to19)
NM_008295	Mus musculus hydroxysteroid dehydrogenase-5, delta<5>-3-beta (Hsd3b5), mRNA	F: (C-IR) 2.43, F: (C-D) 5.64, F: (IR-D) 2.32	F2.25 (Yto0)
NM_008341	Mus musculus insulin-like growth factor binding protein 1 (Igfbp1), mRNA	F: (C-IR) 3.37, F: (C-D) 3.47, F: (IR-D) 2.63	F13.28 (5to11)
NM_008361	Mus musculus interleukin 1 beta (Il1b), mRNA	F: (C-IR) 2.65, F: (C-D) 2.03	U: 3.05 (5to7)
NM_008362	Mus musculus interleukin 1 receptor, type I (Il1r1), mRNA	U: (C-IR) 2.59, F: (IR-D) 2.22	F2.26 (5to19)
NM_008495	Mus musculus lectin, galactose binding, soluble 1 (Lgals1), mRNA	F: (C-IR) 2.65, U: (C-D) 2.32	U: 4.6 (7to11)
NM_008509	Mus musculus lipoprotein lipase (Lpl), mRNA	F: (C-D) 2.05, F: (IR-D) 2.42	F2.64 (5to19)
NM_008745	Mus musculus neurotrophic tyrosine kinase, receptor, type 2 (Ntrk2), mRNA	U: (C-D)+ 2.68	U: 14.81 (Yto0)

5

10

		F: (C-IR) 2.15, F: (C-D) 3.29, F: (IR-D) 2.71	U: 2.2 (YtoM)
NM_009127	Mus musculus stearyl-Coenzyme A desaturase 1 (Scd1), mRNA		
		U: (IR-D) 2.01 F: (C-D) 2.61	U: 3.6 (5to19)
NM_009255	Mus musculus serine protease inhibitor 4 (Spi4), mRNA		
NM_009263	Mus musculus secreted phosphoprotein 1 (Spp1), mRNA	F: (C-IR) 2.04	F2.82 (5to19)
		U: (IR-D) 2.1 F: (C-D) 3.91	F3.29 (7to19)
NM_009344	Mus musculus T-cell death associated gene (Tdag), mRNA		
NM_009345	Mus musculus deoxynucleotidyltransferase, terminal (Dntt), mRNA	U: (C-D) + 3.66	U: 2.43 (YtoO)
		F: (C-IR) 3.13 U: (C-D) 3.23	F8.34 (5to7)
NM_009669	Mus musculus amylase 2, pancreatic (Amy2), mRNA		
NM_009676	Mus musculus aldehyde oxidase 1 (Aox1), mRNA	F: (C-IR) 2.08	U: 2.36 (5to7)
		F: (C-D) 4.15, U: (IR-D) 2.11	F2.93 (5to19)
NM_009744	Mus musculus B-cell leukemia/lymphoma 6 (Bcl6), mRNA		
NM_009864	Mus musculus cadherin 1 (Cdh1), mRNA	F: (C-IR) 2.05	F3.24 (YtoO)
		U: (IR-D) 2.45 F: (C-D) 2.25	F2.13 (Min)
NM_009895	Mus musculus cytokine inducible SH2-containing protein (Cish), mRNA		
		F: (C-IR) 2.61, F: (C-D) 2.33	U: 2.02 (11to19)
NM_009998	Mus musculus cytochrome P450, 2b10, phenobarbital inducible, type b (Cyp2b10), mRNA		
		F: (C-IR) 2.04, U: (IR-D) 2.14	F2.11 (7to11)
NM_010015	Mus musculus decay accelerating factor 1 (Daf1), mRNA		
		F: (C-IR) 2.00, F: (C-D) 2.4	U: 2.89 (5to11)
NM_010062	Mus musculus deoxyribonuclease II alpha (Dnase2a), mRNA		
NM_010107	Mus musculus ephrin A1 (Efna1), mRNA	F: (C-D) 2.18	U: 2.01 (5to7)
		F: (C-IR) 2.18, U: (IR-D) 2.55	F2.28 (7to19)
NM_010187	MusMusculus Fc receptor, IgG, low affinity IIb (Fcgr2b), mRNA		
		U: (C-D) + 2.08	U: 2.42 (5to11)
NM_010225	Mus musculus forkhead box F2 (Foxf2), mRNA		
		U: (C-IR) 2.83, F: (IR-D) 2.17	F3.32 (5to19)
NM_010286	Mus musculus glucocorticoid-induced leucine zipper (Gilz), mRNA		

NM_010324	Mus musculus glutamate oxaloacetate transaminase 1, soluble (Got1), mRNA	F: (C-D) 2.01	F2.08 (5to11)
NM_010354	Mus musculus gelsolin (Gsn), mRNA	U: (C-IR) 2.03	F2.34 (5to19)
NM_010357	Mus musculus glutathione S-transferase, alpha 4 (Gsta4), mRNA	F: (C-IR) 2.17, F: (C-D) 2.93	U:2.11 (5to19)
NM_010361	Mus musculus glutathione S-transferase, theta 2 (Gstt2), mRNA	F: (C-IR) 2.46, F: (C-D) 2.25	U:2.14 (5to19)
NM_010634	Mus musculus fatty acid binding protein 5, epidermal (Fabp5), mRNA	U: (C-IR) 3.17, F: (IR-D) 5.62	F2.84 (5to19)
NM_011087	Mus musculus paired-Ig-like receptor A1 (Pirai), mRNA	F: (C-D)- 2.49	F2.03 (YtoO)
NM_011125	Mus musculus phospholipid transfer protein (Pltp), mRNA	F: (C-IR) 2.01	U:3.1 (YtoO)
NM_011128	Mus musculus pancreatic lipase-related protein 2 (Pnliprp2), mRNA	U: (C-D) 2.35, U: (IR-D) 2.73 F: (C-D) 2.85	U:2.14 (5to11)
NM_011146	Mus musculus peroxisome proliferator activated receptor gamma (Pparg), mRNA	F: (C-IR) 2.17	U:2.68 (5to11)
NM_011375	Mus musculus sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase) (Siat9), mRNA	U: (C-IR) 2.65, U: (C-D) 2.16	F2.12 (5to19)
NM_011579	Mus musculus T-cell specific GTPase (Tgtp), mRNA	U: (C-IR) 2.13 F: (C-D) 2.1	F2.1 (5to19)
NM_011704	Mus musculus vanin 1 (Vnn1), mRNA	U (C-IR) 4.37, U (C-D) 3.14, U (IR-D) 2.37	U:2.87 (5to7)
NM_012006	Mus musculus cytosolic acyl-CoA thioesterase 1 (Ctel), mRNA	F: (C-D) 2.24	U:3.07 (5to7)
NM_013459	Mus musculus adipisin (Adn), mRNA	F: (C-IR) 2.94	U:6.09 (5to11)
NM_013584	Mus musculus leukemia inhibitory factor receptor (Lifr), mRNA	F: (C-IR) 2.31, F: (C-D) 2.46	F3.35 (5to19)
NM_013594	Mus musculus methyl-CpG binding domain protein 1 (Mbd1), mRNA	U: (C-IR) 2.01, U: (C-D) 2.15	F2.35 (5to19)
NM_013623	Mus musculus orosomucoid 3 (Orm3), mRNA	U: (C-D)+ 4.05	U:3.35 (7to19)
NM_013786	Mus musculus hydroxysteroid 17-beta dehydrogenase 9 (Hsd17b9), mRNA	U: (C-D)+ 3.68	F3.08 (YtoM)

			F: (C-IR) 3.7, U: (C-D) 3.14	F4.93 (5to19)
	NM_015763	Mus musculus lipin 1 (lpin1), mRNA		
		Mus musculus complement component 6 (C6), mRNA	F: (C-IR) 2.26, U: (IR-D) 3.29	F2.2 (5to19)
	NM_016704		U: (C-IR) 2.02, F: (IR-D) 2.03	F2.48 (5to19)
	NM_016847	Mus musculus arginine vasopressin receptor 1A (Avpr1a), mRNA		
			U: (IR-D) 2.73 F: (C-D) 4.72	F2.26 (YtoO)
	NM_016875	Mus musculus Y box protein 2 (Ybx2), mRNA		
		Mus musculus phosphodiesterase 3A, cGMP inhibited (Pde3a), mRNA	F: (C-IR) 2.35, F: (C-D) 2.43	U:2.15 (5to19)
5	NM_018779		U: (C-IR) 2.18	U:2.25 (YtoM)
	NM_018861	Mus musculus solute carrier family 1 (glutamate/neutral amino acid transporter), member 4 (Slc1a4), mRNA		
		Mus musculus cytochrome P450, 39a1 (oxysterol 7alpha-hydroxylase) (Cyp39a1-pending), mRNA	U: (C-D)+ 2.54	F3 (7to19)
	NM_018887		U: (C-IR) 2.06	U:2.6 (5to11)
	NM_019415	Mus musculus solute carrier family 12, member 3 (Slc12a3), mRNA		
		Mus musculus acetyl-Coenzyme A synthetase 1 (AMP forming) (Acas1), mRNA	F: (C-IR) 2.03, F: (C-D) 2.11	U:2.07 (YtoM)
	NM_019811		U: (C-D) 2.05 F: (C-D) 2.29	F2.03 (11to19)
10	NM_019922	Mus musculus cartilage associated protein (Crtp), mRNA		
		Mus musculus aldehyde reductase (aldose reductase)-like 6 (Aldrl6), mRNA	U: (C-IR) 2.51 F: (C-D) 2.15	U:2.18 (YtoO)
	NM_019977		U: (C-IR) 2.06, U: (C-D) 2.23, U: (IR-D) 2.12	U:2.47 (YtoO)
	NM_019992	Mus musculus BCR downstream signaling 1 (Brdgl-pending), mRNA		
			U: (C-D) 2.05, U: (IR-D) 2.32 F: (C-D) 4.69	U:3.35 (5to11)
	NM_020277	Mus musculus long transient receptor potential-related channel 5 (Ltrpc5-pending), mRNA		
			F: (C-IR) 2.84, F: (C-D) 2.36, U: (IR-D) 2.6	F2.32 (5to19)
	NM_020564	Mus musculus sulfotransferase-related protein SULT-X1 (Sult-x1), mRNA		
15	NM_020568	Mus musculus plasma membrane associated protein, S3-12 (S3-12-pending), mRNA	U: (C-D)+ 2.12	U:6.5 (YtoO)



435

NM 021468	Mus musculus uncl3 homolog (C. elegans) 1 (Unc13h1), mRNA	F: (C-D)- 2.18	U: 3.58 (MtoO)
NM 022331	Mus musculus homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1 (Herpud1), mRNA	U: (C-IR) 3.00, U: (C-D) 2.29	F3.44 (5to19)
NM 023184	Mus musculus Kruppel-like factor 15 (Klf15), mRNA	U: (C-IR) 2.34	F2.87 (5to11)
NM 023455	Mus musculus camello-like 4 (Cml4), mRNA	F: (C-IR) 2.39, F: (C-D) 2.04	U: 2.75 (5to19)
NM 023740	Mus musculus RIKEN cDNA 1500015N03 gene (1500015N03Rik), mRNA	F: (C-IR) 1.7, F: (C-D) 2.35, U: (IR-D) 2.52	U: 2.04 (5to11)
NM 025404	Mus musculus RIKEN cDNA 1110036H21 gene (1110036H21Rik), mRNA	F: (C-IR) 2.24, F: (C-D) 2.03	F3.11 (5to11)
NM 025429	Mus musculus serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1a (Serpina1a), mRNA	F: (C-IR) 3.51, F: (C-D) 3.01	U: 4.44 (5to19)
NM 026104	Mus musculus RIKEN cDNA 1700095F04 gene (1700095F04Rik), mRNA	F: (C-IR) 2.22	F2.72 (5to7)
NM 029813	Mus musculus RIKEN cDNA 2210418010 gene (2210418010Rik), mRNA	F: (C-D) 2.4	F2:28 (5to19)
NM 033373	Mus musculus type I intermediate filament cytokeratin (Haik1-pending), mRNA	U: (C-D)+ 7.74	F2.05 (YtoO)
NM 053215	Mus musculus RIKEN cDNA 0610033E06 gene (0610033E06Rik), mRNA	F: (C-IR) 1.98, F: (C-D) 3.23	F2.18 (5to19)
U6 7189	MMU67189 Mus musculus G protein signaling regulator RGS16 (rgs16) mRNA, complete cds	U: (C-IR) 3.17	U: 2.23 (YtoM)
U7 0139	MMU70139 Mus musculus probable nocturnin protein mRNA, partial cds	U: (C-D) 3.08, U: (IR-D) 2.08	F2.05 (5to7)
X0 3796	MMALDCR5 Mouse mRNA 5'-region for aldolase C (aa 1-227)	F: (C-D)- 2.14	U: 2.61 (YtoM)

5

10

15

Table 201

## Pairwise Differential Expression Comparisons for Selected Mouse Genes

Gene	Age 5-7	Age 5-11	Age 15-19	Age 7-14	Age 7-19	Age 11-19	Age Y-M	Age Y-O	Age M-O
AK002979	U1.63	U2.31	U2.94	U1.42	U1.81	U1.27	U2.90	U2.36	F1.23
AK004387	F1.79	F2.93	F3.29	F1.64	F1.84	F1.12	F1.40	F2.33	F1.67
NM_007702	U1.22	F1.07	U2.59	U1.30	U2.13	U2.78	U16.0 9	U57.0 1	U3.54
U67189	F2.04	F3.57	F1.91	F1.75	U1.07	U1.86	F2.25	F1.02	U2.21

Differential expression is set forth as the ratio of greater expression level to lesser expression level for the indicated time points. The direction of the change of expression is indicated by "F" (favorable, i.e., younger>older) or "U" (unfavorable, i.e., older>younger). Significant differences (at least two fold) are bold faced.

Note that in identifying a mouse gene as favorable, unfavorable, or mixed, only the significant (at least two fold) differentials are considered.

For the first six comparisons, the time points are weeks, e.g., "7\_19" is 7 weeks vs. 19 weeks.

For the last three comparisons, the "Y", "M" and "O" represent

Y (young)= expression at 118 days

M (medium)= average of expression at 207 and 403 days

O (old) = average of expression at 558 and 725 daus

**Example 2**

The Amersham CodeLink™ Uniset Mouse I Bioarray Platform was used (example 1) to identify differences in liver gene expression in aging mice. The mice were fed normal chow and were sacrificed at ages ranging from 35 to 725 days. A total of 190 genes were differentially expressed by at least a 2-fold magnitude (Master Table 1). Analysis of the differentially expressed genes identified CIDE-A as the most differentially expressed gene in liver during this age span. The level of mouse CIDE-A expression in these mice is shown in figure 1.

No CIDE-A expression was detected at 35 to 56 days of age (expression level less than 0.2). The expression of CIDE-A was barely detectable at 118 and 207 days of age (0.36 +/- 0.23 and 0.23 +/- 0.10, respectively). However, CIDE-A is readily detected at 403 days of age (3.5 +/- 1.99) and the level of expression continues to increase to 7.7 (+/- 0.12) at 558 days of age. Taken together, the level of CIDE-A expression in liver increases at least 38-fold as the mouse progresses from 35 days of age to maximal expression at 558 days of age (7.7 +/- 0.12). See Figure 1.

The differentially expressed gene CIDE-A was subjected to further analysis.

**Northern analysis**

Total RNA (10 ug) from the appropriate tissues was resolved by denaturing agarose gel electrophoresis, transferred to positively charged nylon membrane, hybridized with the [ $\alpha$ - $^{32}$ P]dCTP-labeled mouse CIDE-A cDNA (Random Primed DNA Labeling Kit, Roche, Indianapolis, IN) and exposed to Bio-Max MR film (Eastman Kodak Co., Rochester, NY).

**Immunoblot analysis**

Liver and heart tissue (100mg) was homogenized in 0.5ml phosphate buffered saline containing 7.5ul protease inhibitor cocktail (Sigma #P8340, St. Louis, MO). The samples were centrifuged for 5 min at 10,000 x g. The supernatant was

collected and protein concentration determined (Bio-Rad Laboratories #500-0006, Hercules, CA). Sixty micrograms of each extract was electrophoresed on a 12.5% SDS-polyacrylamide gel as described previously (25 Bowen). The resolved proteins were transferred to a nitrocellulose membrane and immunoblotted using a rabbit anti-mouse CIDE-A polyclonal antibody (QED Bioscience Inc., San Diego, CA) as previously described, see Kelder, B., Richmond, C., Stavnezer, E., List, E.O. and Kopchick, J.J., "Production, characterization and functional activities of v-Ski in cultured cells," Gene, 202:1521 (1997), and a goat anti-rabbit IgG polyclonal antibody conjugated to horseradish peroxidase.

#### *Liver Histology*

Liver tissues fixed in 4% paraformaldehyde were embedded in Tissue Path (Fisher Scientific, Pittsburgh, PA). Representative sections were prepared from each liver block, placed on a slide, subjected to H&E staining and evaluated by light microscopy. The percent white space was determined as a quantification of the level of steatosis.

*Liver steatosis is observed in the CIDE-A expressing older mice.*

We performed histological examinations on H&E stained liver sections prepared from mice of various ages to determine if increased CIDE-A expression effected any noticeable changes in the livers of these mice. Among other changes, we noticed an increased level of lipid accumulation within hepatocytes at 725 days of age. There was also an increased level of steatosis in liver tissue isolated from 558 day-old mice but the level of lipid accumulation did not approach that seen at 725 days.

*CIDE-A is expressed at an early age in liver of high-fat fed type-II diabetic mice exhibiting liver steatosis.*

Due to the correlation of increased CIDE-A expression and liver steatosis with increasing age, we investigated whether CIDE-A expression would also be increased in other models of liver steatosis. We utilized a mouse model of diet-induced obesity, hyperinsulinemia and type-II diabetes, see Surwit, R.S., Kuhn, C.M., Cochrane, C., McCubbin, J.A., Feinglos, M.N. (1988) "Diet-induced type-II diabetes in C57BL/6J mice," Diabetes 37:1163-1167. Mice were weaned onto either a normal diet or a high-fat diet for up to 26 weeks. Representative mice were sacrificed after 2, 4, 8, 16 and 26 weeks on the diet (35, 49, 77, 133 and 203 days of age) and CIDE-A expression levels were determined by DNA microarray analysis (Fig. 2).

We performed histological examinations on H&E stained liver sections prepared from control and type-II diabetic mice after 2, 16 and 26 weeks of high fat diet feeding (diet started at 3 weeks of age) to assess the degree of diet-induced liver steatosis (Fig. 3). The percent white space of each liver sample was determined by a histomorphometric profiling method using machine vision. H&E stained liver sections isolated from mice fed a normal diet at 56, 558 and 725 days of age shows the accumulation of lipid in liver hepatocytes of older mice.

Histological analysis indicated that diabetic liver hepatocytes accumulate a small amount of lipid as soon as 2 weeks on a high-fat diet and by 8 weeks, liver tissue isolated from high fat-fed mice contain significantly more lipid than their control counterparts. Severe liver steatosis is observed in liver tissues isolated from mice fed the high-fat diet for 16 weeks and is even more pronounced after 26 weeks of high-fat feeding. The percent white space in these livers is 31.6 and 53.2%, respectively. In comparison, the percent white space in liver tissue of mice fed the normal diet for 16 and 26 weeks is 10.3 and 12.2%, respectively. In addition, liver tissue isolated from 16 week high-fat fed hyperinsulinemic mice demonstrate liver steatosis but at a much lower level compared to its diabetic counterpart.

*Correlation of CIDE-A gene expression and cell protein levels.*

Since mRNA levels may not be indicative of the actual level of protein found in the tissue, we performed immunoblot analysis on heart and liver tissue isolated from control, hyperinsulinemic and type-II diabetic mice to confirm the increased CIDE-A levels.

*Expression of genes involved in caspase-dependent apoptosis*

Several groups have reported increase gene expression of members of the Caspase-dependent apoptotic pathway such as the FAS death receptor and Fas ligand in hepatocyte steatosis. See Feldstein, supra; Canbay A, Feldstein AE, Higuchi H, Werneburg N, Grambihler A, Bronk SF, Gores GJ. (2003) Kupffer cell engulfment of apoptotic bodies stimulates death ligand and cytokine expression. *Hepatology* 38:1188-1198. We therefore examined the levels of expression of genes involved in this pathway by DNA microarray analysis. A summary of the expression for the genes represented on the microarray is presented in Table 201.

*Caspase-3 and -7*

Expression levels of Caspase 3 and 7 both decrease from control to hyperinsulinemic to type-II diabetic. But immunohistochemistry on NASH liver sections and a rabbit antibody that recognizes a "neoepitope" (new epitope that is generated upon caspase 3 and 7 cleavage and activation) demonstrated increases in Caspase 3 and 7 activation. The decrease in caspase 3 and 7 gene expression may be an attempt by the cell to reduce apoptotic signaling within the cell (negative feedback).

*Apoptosis in Liver*

The level of apoptosis in liver may appear minor. However the rapid phagocytosis of apoptotic bodies makes the detection of such bodies in tissue extremely difficult, see Savill, J. (2000) Apoptosis in resolution of inflammation. *Kidney Blood*

Press. Res. 23:173-174. A 4% rate of apoptosis would lead to a 25% reduction in liver tissue in 72 hours, see Schulte-Hermann, R., Bursch, W., Grasl-Kraupp, B. (1995) Active cell death (apoptosis) in liver biology and disease. Prog. Liver Dis. 13:1-35. Therefore, while it may be possible to observe only a small proportion of the ongoing apoptosis, the ongoing cell death may lead to major liver dysfunction.

#### Alternative Model

While increased apoptosis may be a contributing factor to liver dysfunction, we would like to put forth an alternate model for CIDE-A function in liver. In this model: CIDE-A is a part of a redundant apoptotic pathway. According to this model, in the early time points of the genesis of insulin resistance and Type-II diabetes, the liver is capable of managing liver steatosis by the primary caspase-activated apoptotic pathway to eliminate unwanted (lipid accumulating) hepatocytes. However, as the disease progresses (and lipid accumulates), the primary apoptotic pathway becomes overwhelmed (or non-functional) and a secondary (CIDE-A based) pathway is employed as an emergency (last-ditched) effort to maintain liver homeostasis. However, this secondary, redundant apoptotic pathway that includes CIDE-A, is either not as efficient or incapable of eliminating the overwhelming lipid accumulation and eventual pathogenesis results.

It is possible that the apoptosis-induced cell death of lipid-containing hepatocytes results in the release of intracellular lipid and the concurrent extracellular liver lipid accumulation. This accumulation may then affect liver functions.

442

Table 201. Expression of genes involved in caspase-dependent apoptosis. The Amersham CodeLink™ Uniset Mouse I Bioarray Platform was used to determine the expression levels of control mice or high-fat fed mice exhibiting hyperinsulinemia or type-II diabetes after 16 week of feeding (N=2). Raw expression values are stated, those resulting in 2-fold or greater differential expression are boldfaced.

	Control	Hyperinsulinemic	Type-II Diabetic
5			
	<b>0.28</b> +/- 0.00	0.23 +/- 0.01	0.14 +/- 0.01
	<b>2.22</b> +/- 0.07	<b>2.54</b> +/- 0.08	<b>3.31</b> +/- 0.30
10	<b>1.80</b> +/- 0.16	2.08 +/- 0.13	1.61 +/- 0.08
	<b>1.19</b> +/- 0.21	1.03 +/- 0.05	1.09 +/- 0.11
	<b>2.86</b> +/- 0.15	<b>3.00</b> +/- 0.43	2.27 +/- 0.12
	<b>0.72</b> +/- 0.03	0.93 +/- 0.06	0.55 +/- 0.14
	<b>1.17</b> +/- 0.07	1.45 +/- 0.09	1.24 +/- 0.06
15	<b>2.03</b> +/- 0.14	<b>1.33</b> +/- 0.29	<b>1.45</b> +/- 0.43
	<b>14.67</b> +/- 0.71	<b>17.41</b> +/- 2.43	<b>18.00</b> +/- 1.96
	<b>4.01</b> +/- 0.11	<b>3.43</b> +/- 0.66	<b>2.89</b> +/- 0.14
	<b>3.81</b> +/- 0.39	<b>3.44</b> +/- 0.10	<b>3.37</b> +/- 0.63
	<b>0.56</b> +/- 0.00	0.73 +/- 0.02	0.56 +/- 0.03
20	<b>49.46</b> +/- 0.01	<b>53.79</b> +/- 6.79	<b>54.59</b> +/- 4.64
	<b>0.26</b> +/- 0.02	0.19 +/- 0.00	0.20 +/- 0.03
	<b>1.34</b> +/- 0.01	<b>1.44</b> +/- 0.13	<b>1.76</b> +/- 0.19
	<b>0.48</b> +/- 0.04	<b>0.55</b> +/- 0.07	<b>0.46</b> +/- 0.01
25	<b>1.32</b> +/- 0.06	1.29 +/- 0.08	1.38 +/- 0.07
	<b>2.77</b> +/- 0.29	<b>3.58</b> +/- 0.06	<b>3.48</b> +/- 0.15
	<b>0.37</b> +/- 0.05	0.35 +/- 0.08	0.45 +/- 0.05
	<b>0.29</b> +/- 0.00	<b>0.31</b> +/- 0.01	0.21 +/- 0.03
	<b>0.21</b> +/- 0.00	0.15 +/- 0.01	0.15 +/- 0.02



## References

1. Semsei I. (2000) On the nature of aging. Mech Aging Dev 117:93-108.
2. Sohal, RS, Weindruch, R. (1998) Oxidative stress, caloric restriction, and aging. Science 273:59-63.
3. Finch, CE, Revkun, G. (2001) The genetics of aging. Annu. Rev. Genom. Hum. Genet. 2:435-462.
4. Roth, GS, Lasnikov, V, Lesnikov, M, Ingram, DK, Land, MA (2001) Dietary caloric restriction prevents the age-related decline in plasma melatonin levels of rhesus monkeys. J Clin Endocrinol Metab. 86:3292-5.
5. Roth GS, Lane MA, Ingram DK, Mattison JA, Elahi D, Tobin JD, Muller D, Metter EJ (2002) Biomarkers of caloric restriction may predict longevity in humans. Science. 297:811-813.
6. Walford RL, Mock D, Verdery R, MacCallum T. (2002) Calorie restriction in biosphere 2: alterations in physiologic, hematologic, hormonal, and biochemical parameters in humans restricted for a 2-year period. J Gerontol A Biol Sci Med Sci 57:211-24.
7. Kenyon C, Chang J, Gensch E, Rudner A, Tabtiang R. (1993) A *C. elegans* mutant that lives twice as long as wild type. Nature 366:461-464.
8. Lin, K, Dorman, JB, Rodan, A, Kenyon, C. (1997). *daf-16*: an HNF-3/Forkhead family member that can function to double the life-span of *Caenorhabditis elegans*. Science 278, 1319-1322.
9. Clancy DJ, Gems D, Harshman LG, Oldham S, Stocker H, Hafen

12. Ramaswamy S, Nakamura N, Sansal I, Bergeron L, Sellers WR. (2002) A novel mechanism of gene regulation and tumor suppression by the transcription factor FKHR. *Cancer Cell* 2002 2:81-91.

5 13. Hekimi, S, Guarente, L. (2003) Genetics and the specificity of the aging process. *Science* 299:1351-1354.

14. Brown-Borg, HM, Borg, KE, Meliska, CJ, Bartke, A. (1996) Dwarf mice and the aging process. *Nature* 384:33.

10 15. Flurkey K, Papaconstantinou J, Miller RA, Harrison DE. (2001) Lifespan extension and delayed immune and collagen aging in mutant mice with defects in growth hormone production. *Proc Natl Acad Sci USA* 98:6736-6741.

16. Zhou, Y, Xu, BC, Maheshwari, HG, He, L, Reed, M, Lozykowski, M, Okada, S, Cataldo, L, Coschigano, K, Wagner, TE, 15 Baumann, G, Kopchick, JJ. (1997) A mammalian model for Laron syndrome produced by targeted disruption of the mouse growth hormone receptor/binding protein gene (the Laron mouse). *Proc. Nat. Acad. Sci. USA* 94:13215-13220.

17. Coschigano, K, Clemmons, D, Bellush, LL, Kopchick, JJ. 20 (2000) Assessment of growth parameters and life-span of GHR/BP gene-disrupted mice. *Endocrinology* 141:2608-2613.

17a. Coschigano, KT, Holland, AN, Riders, ME, List, EO, Flyvberg, A, Kopchick, JJ, Deletion, but not antagonism, of the 25 mouse growth hormone receptor results in severely decreased body weights, insulin and IGF-1 levels and increased lifespan, *Endocrinology* (electronically published May 30, 2003 as doi:10.1210/en.2003-0374).

30 18. Holzenberger M, Dupont J, Ducos B, Leneuve P, Geloën A, Even PC, Cervera P, Le Bouc Y. (2003) IGF-1 receptor regulates lifespan and resistance to oxidative stress in mice. *Nature* 421:182-187.

35 19. Migliaccio E, Giorgio M, Mele S, Pelicci G, Reboldi P, Pandolfi PP, Lanfranccone L, Pelicci PG. (1999) The p66shc

adaptor protein controls oxidative stress response and life span in mammals. Nature 402:309-313.

20. Bartke A, Wright JC, Mattison JA, Ingram DK, Miller RA, Roth GS. (2001) Extending the lifespan of long-lived mice.

Nature 414:412.

21. Weindruch R, Kayo T, Lee CK, Prolla TA. (2002) Gene expression profiling of aging using DNA microarrays. Mech Aging Dev 123:177-193.

22. Lee CK, Allison DB, Brand J, Weindruch R, Prolla TA. (2002) Transcriptional profiles associated with aging and middle age-onset caloric restriction in mouse hearts. Proc Natl Acad Sci USA 99:14988-14993.

23. Prolla TA. (2002) DNA microarray analysis of the aging brain. Chem Senses 27:299-306.

Citation of documents herein is not intended as an admission that any of the documents cited herein is pertinent prior art, or an admission that the cited documents is considered material to the patentability of any of the claims of the present application. All statements as to the date or representation as to the contents of these documents is based on the information available to the applicant and does not constitute any admission as to the correctness of the dates or contents of these documents.

The appended claims are to be treated as a non-limiting recitation of preferred embodiments.

In addition to those set forth elsewhere, the following references are hereby incorporated by reference, in their most recent editions as of the time of filing of this application: Kay, Phage Display of Peptides and Proteins: A Laboratory Manual; the John Wiley and Sons Current Protocols series, including Ausubel, Current Protocols in Molecular Biology; Coligan, Current Protocols in Protein Science; Coligan, Current Protocols in Immunology; Current Protocols in Human Genetics; Current Protocols in Cytometry; Current Protocols in Pharmacology; Current Protocols in Neuroscience; Current Protocols in Cell Biology; Current Protocols in Toxicology; Current Protocols in Field Analytical Chemistry; Current Protocols in Nucleic Acid Chemistry; and Current Protocols in Human Genetics; and the following Cold Spring Harbor Laboratory publications: Sambrook, Molecular Cloning: A Laboratory Manual; Harlow, Antibodies: A Laboratory Manual; Manipulating the Mouse Embryo: A Laboratory Manual; Methods in Yeast Genetics: A Cold Spring Harbor Laboratory Course Manual; Drosophila Protocols; Imaging Neurons: A Laboratory Manual; Early Development of *Xenopus laevis*: A Laboratory Manual; Using Antibodies: A Laboratory Manual; At the Bench: A Laboratory Navigator; Cells: A Laboratory Manual; Methods in Yeast Genetics: A Laboratory Course Manual; Discovering Neurons: The Experimental Basis of Neuroscience; Genome

447

Analysis: A Laboratory Manual Series ; Laboratory DNA Science; Strategies for Protein Purification and Characterization: A Laboratory Course Manual; Genetic Analysis of Pathogenic Bacteria: A Laboratory Manual; PCR Primer: A Laboratory Manual; Methods in Plant Molecular Biology: A Laboratory Course Manual ; Manipulating the Mouse Embryo: A Laboratory Manual; Molecular Probes of the Nervous System; Experiments with Fission Yeast: A Laboratory Course Manual; A Short Course in Bacterial Genetics: A Laboratory Manual and Handbook for Escherichia coli and Related Bacteria; DNA Science: A First Course in Recombinant DNA Technology; Methods in Yeast Genetics: A Laboratory Course Manual; Molecular Biology of Plants: A Laboratory Course Manual.

All references cited herein, including journal articles or abstracts, published, corresponding, prior or otherwise related U.S. or foreign patent applications, issued U.S. or foreign patents, or any other references, are entirely incorporated by reference herein, including all data, tables, figures, and text presented in the cited references. Additionally, the entire contents of the references cited within the references cited herein are also entirely incorporated by reference.

Reference to known method steps, conventional methods steps, known methods or conventional methods is not in any way an admission that any aspect, description or embodiment of the present invention is disclosed, taught or suggested in the relevant art.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying knowledge within the skill of the art (including the contents of the references cited herein), readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present invention. Therefore, such adaptations and modifications are intended to

be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the present specification is to be interpreted by the skilled artisan in light of the teachings and guidance presented herein, in combination with the knowledge of one of ordinary skill in the art.

Any description of a class or range as being useful or preferred in the practice of the invention shall be deemed a description of any subclass (e.g., a disclosed class with one or more disclosed members omitted) or subrange contained therein, as well as a separate description of each individual member or value in said class or range.

The description of preferred embodiments individually shall be deemed a description of any possible combination of such preferred embodiments, except for combinations which are impossible (e.g., mutually exclusive choices for an element of the invention) or which are expressly excluded by this specification.

If an embodiment of this invention is disclosed in the prior art, the description of the invention shall be deemed to include the invention as herein disclosed with such embodiment excised.

CLAIMS

1. A method of (I) reducing a rate of biological aging in a human subject, and/or(II) delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or (III) protecting against an age-related (senescent) disease, which comprises

administering to the subject a protective amount of an agent which is

(1) a polypeptide which is substantially structurally identical or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1A, or (b) selected from the group consisting of human proteins within at least one of the human protein classes set forth in master table 2, subtable 2A,

or

(2) an expression vector encoding the polypeptide of (1) above and expressible in a human cell, under conditions conducive to expression of the polypeptide of (1);

where said agent reduces a rate of biological aging in said subject, and/or delays the time of onset, or reduces the severity, of an undesirable age-related phenotype in said subject, and/or protects against an age-related disease.

2. A method of (I) reducing a rate of biological aging in a human subject, and/or(II) delaying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or (III) protecting against an age-related (senescent) disease, which comprises

administering to the subject a protective amount of an agent which is

450

(1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B, or (b) selected from the group consisting of human proteins belonging to at least one of the human protein classes set forth in master table 2, subtable 2B,

(2) an anti-sense vector which inhibits expression of said polypeptide in said subject,

where said agent reduces a rate of biological aging in said subject, and/or delays the time of onset, or reduces the severity, of an undesirable age-related phenotype in said subject, and/or protects against an age-related disease.

3. A method of determining a biological age of a human subject, or a rate of biological aging of a human subject, which comprises

assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1A, or (b) selected from the group consisting of human proteins within at least one of the human protein classes set forth in master table 2, subtable 2A,

and inversely correlating the level of expression of said marker gene with a biological age or a rate of biological aging of said patient.



4. A method of determining a biological age of a human subject, or a rate of biological aging of a human subject, which comprises

5 assaying tissue or body fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein  
10 which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B, or (b) selected from the group consisting of human proteins belonging to at least one of the human protein classes set forth in master table 2, subtable 2B,

15 and directly correlating the level of expression of said marker gene with a biological age or a rate of biological aging of said subject.

20 5. The method of claims 1 or 2 in which (I) applies.

6. The method of claims 1 or 2 in which (II) applies.

7. The method of claims 1 or 2 in which (III) applies.

25 8. The method of claim 5 in which biological age is measured by a biomarker.

30 9. The method of claim 8 in which the marker is a simple biomarker.

10. The method of claim 8 in which the marker is a composite biomarker.

35 11. The method of claim 5 in which the affected biological age is the overall biological age of the subject.

452

12. The method of claim 5 in which the affected biological age is the biological age of a body system of the subject.

13. The method of claim 5 in which the affected biological age is the biological age of an organ of the subject.

14. The method of claim 13 in which the organ is the liver.

15. The method of claim 8 in which at least one marker is the level of a biochemical in the blood of the subject.

16. The method of claim 15 in which the biochemical is growth hormone or IGF-1.

17. The method of any one of claims 1-16 in which (a) applies.

18. The method of any one of claims 1-17 in which the reference protein is a human protein.

19. The method of any one of claims 1-17 in which the reference protein is a mouse protein.

20. The method of any one of claims 3 or 4 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

21. The method of any one of claims 3 or 4 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.

22. The method of any one of claims 1-21 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

23. The method of any one of claims 1-22 in which said

453

polypeptide is at least 90% identical to said reference protein.

24. The method of claim 23 in which said polypeptide is identical to said reference protein.

25. The method of any one of claims 1-24 in which the E-value cited for the reference protein in Master Table 1 is not more than  $e^{-6}$ .

26. The method of claim 25 in which the E-value cited for the reference protein in Master Table 1 is less than  $e^{-10}$ .

27. The method of claim 26 in which the E value calculated by BLASTN or BLASTX is than  $e^{-15}$ , more preferably less than  $e^{-20}$ , still more preferably less than  $e^{-40}$ , even more preferably less than  $e^{-60}$ , considerably more preferably less than  $e^{-80}$ , and most preferably less than  $e^{-100}$ .

28. The method of claims 2 or 4, or of any of claims 5-27 to the extent dependent on 2 or 4, in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.

29. The method of claims 2 or 4, or of any of claims 5-27 to the extent dependent on 2 or 4, in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.

30. The method of claims 2 or 4, or of any of claims 5-27 to the extent dependent on 2 or 4, in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.

31. The method of claim 30 in which said organic molecule is identifiable as a molecule which binds said polypeptide by

454

screening a combinatorial library.

32. The method of any one of claims 2 or 4, or of any of claims  
5-31 to the extent dependent on 2 or 4, in which the marker  
5 protein is CIDE-A.

10

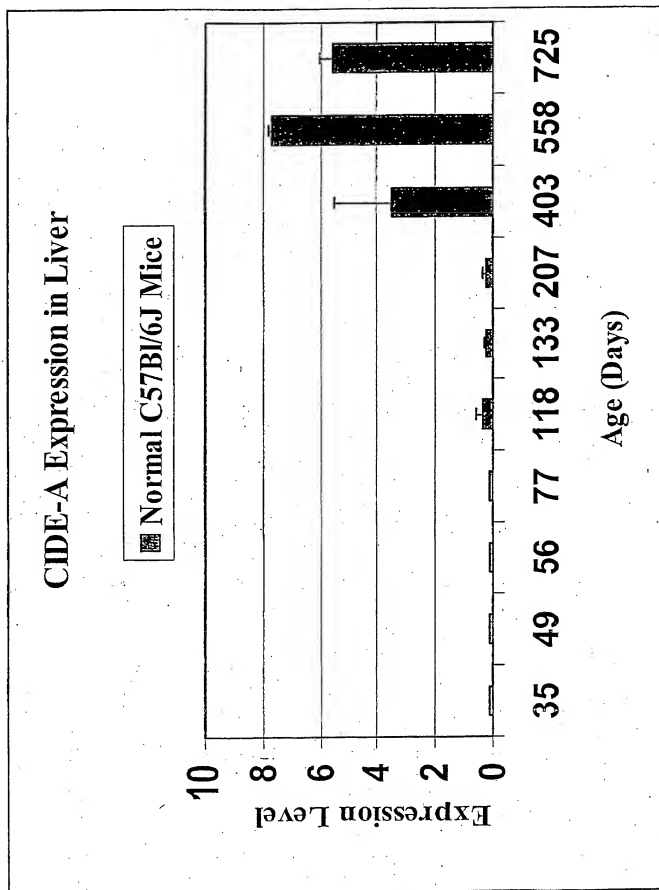


FIGURE 1

### Elevated CIDE-A Expression in Type-II Diabetes

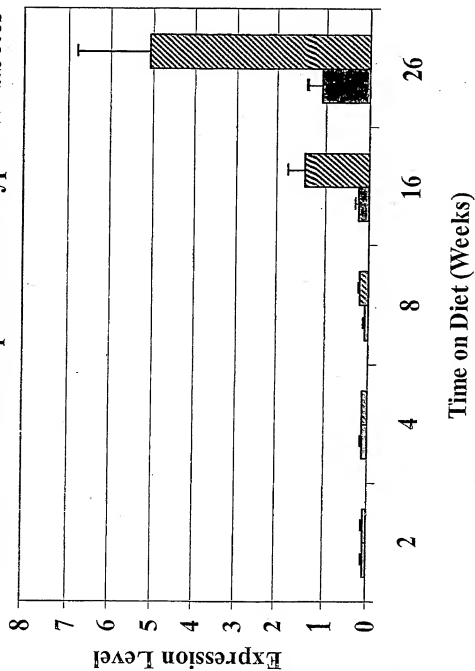


FIGURE 3

